

University of Dundee

## Whole-body magnetic resonance angiography

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## Whole-body magnetic resonance angiography

Weir-McCall, J. R., Bonnici-Mallia, M., Ramkumar, P. G., Nath, A. F. & Houston, J. G. 18 Jul 2018 In : Clinical Radiology. DOI: 10.1016/j.crad.2018.05.032

### Introduction

Vascular disease, whether it be atherosclerosis, inflammatory or hereditary vasculitide, is a systemic disorder with disease in one territory predictive of disease in another.

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of patients without. Methods The U.S. Registry for FMD involves 12 clinical centers. This analysis included clinical history, diagnostic, and therapeutic procedure results for 921 FMD patients enrolled in the registry as of October 17, 2014. Results Aneurysm occurred in 200 patients (21.7%) and dissection in 237 patients (25.7%); in total, 384 patients (41.7%) had an aneurysm and/or a dissection by the time of FMD diagnosis. The extracranial carotid, renal, and intracranial arteries were the most common sites of aneurysm; dissection most often occurred in the extracranial carotid, vertebral, renal, and coronary arteries. FMD patients with dissection were younger at presentation (48.4 vs. 53.5 years of age, respectively;  $p < 0.0001$ ) and experienced more neurological symptoms and other end-organ ischemic events than those without dissection. One-third of aneurysm patients (63 of 200) underwent therapeutic intervention for aneurysm repair. Conclusions Patients with FMD have a high prevalence of aneurysm and/or dissection prior to or at the time of FMD diagnosis. Patients with dissection were more likely to experience ischemic events, and a significant number of patients with dissection or aneurysm underwent therapeutic procedures for these vascular events. Because of the high prevalence and associated morbidity in patients with FMD who have an aneurysm and/or dissection, it is recommended that every patient with FMD undergo one-time cross-sectional imaging from head to pelvis with computed tomographic angiography or magnetic resonance angiography.", "author" : [ { "dropping-particle" : "", "family" : "Kadian-Dodov", "given" : "Daniella", "non-dropping-particle" : "", "parse-names" :

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Cardiac involvements in TA is due to the consequences of the vascular lesions as well as the primary pathology of the heart. The disease activity of TA is known to influence the prognosis of TA. We hypothesized that the cardiovascular involvement of TA is related to the disease activity. We evaluated the cardiovascular manifestations of TA, and we assessed their relation to the disease activity of TA. Two hundred four patients were diagnosed with TA from September, 1994 to March, 2009 according to the diagnostic criteria of the 1990 American College of Rheumatology. Their clinical features and the laboratory, angiographic and echocardiographic findings were retrospectively reviewed. The group with active disease activity was defined as satisfying one of the following criteria: i) an elevated ESR or CRP level, ii) thickened arterial wall with mural enhancement on CT or MR angiography, and iii) carotidynia at the time of the initial diagnosis. One hundred thirty nine patients (69.2%) were classified as the active group. The cardiovascular signs and symptoms were not generally

different between the active and inactive groups. The active TA patients had more frequent involvement of the ascending aorta and the aortic arch and its main branches than did the inactive group. The active group showed a higher incidence of significant aortic valve regurgitation and pulmonary hypertension, and a higher level of NT-proBNP. These findings suggest that disease activity plays an important role for the cardiovascular manifestations of TA. The TA patients with higher activity have more cardiovascular morbidity compared to the TA patients with low disease activity. Wu00a9 2011 Elsevier Ireland Ltd. All rights reserved.",

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dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Kim", "given" : "Duk Kyung", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "International Journal of Cardiology", "id" : "ITEM-3", "issue" : "1", "issued" : { "date-parts" : [ [ "2012" ] ] }, "page" : "14-20", "publisher" : "Elsevier Ireland Ltd", "title" : "Cardiovascular manifestations of Takayasu arteritis and their relationship to the disease activity: Analysis of 204 Korean patients at a single center", "type" : "article-journal", "volume" : "159" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=82df35c7-326b-448f-970b-71fc5aa711c6" ] ] }, "mendeley" : { "formattedCitation" : "<sup><sup>1</sup>Wu2013<sup>3</sup></sup>", "plainTextFormattedCitation" : "1Wu20133", "previouslyFormattedCitation" : "<sup><sup>1</sup>Wu2013<sup>3</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }} Despite this, routine clinical assessment is typically restricted to a single vascular territory or, when multisite assessment is required, will be performed with multiple investigations over multiple visits to the hospital. A routine approach to the global detection and 'staging' of vascular disease has yet to be ingrained in the vascular assessment. Part of this is the difficulty in performing whole body staging and stratification of vascular disease - ultrasound cannot adequately visualize the deeper vessels, whole body CT involves radiation exposure, and historically, technical limitations have restricted MRI to single sites. However while the former remain true, the latter

has changed substantially in recent years. Advances in scanner hardware, the spatial and temporal resolution of modern sequences, table length, and the ability to scan during active table movement, means whole body magnetic resonance angiography (WB-MRA) is now feasible and practicable in a routine clinical environment.

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technique provides a comprehensive non-invasive approach for morphological screening  
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"<sup><sup>4</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-

style-language/schema/raw/master/csl-citation.json" }} This article will explore the technique for WB-MRA, the analysis of the data obtained and the clinical scenarios in which WB-MRA should be considered.

## WB - MRA Technique

WB-MRA has been described using both 1.5T and 3T clinical scanners, with the only hardware requirements being surface coils to cover the whole body, a dual pump injector system capable of separate contrast and saline injections, and a table with sufficient reach as to allow full body coverage.

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cases. CONCLUSIONS: Even in an asymptomatic cohort of middle-aged predominantly male individuals, atherosclerotic disease is not uncommon and is detectable by whole-body MRI.

MAIN MESSAGES: Wu2022 In middle-aged predominantly male individuals, atherosclerotic disease is not uncommon. Wu2022 Even in an asymptomatic collective, approximately one fourth had vascular abnormalities. Wu2022 Using whole-body MR angiography (MRA), 99.8% of

2,070 vessel segments could be evaluated.", "author" : [ { "dropping-particle" : "", "family" :

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enhanced MR angiography with iPAT(2) is feasible for whole-body applications and allows acquisition of 3D data sets with adequate spatial resolution within short measurement times, facilitating a single injection of contrast material.", "author" : [ { "dropping-particle" : "", "family" : "Fenchel", "given" : "Michael", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Doering", "given" : "Joerg", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Seeger", "given" : "Achim", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Kramer", "given" : "Ulrich", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Rittig", "given" : "Kilian", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Klumpp", "given" : "Bernhard", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Claussen", "given" : "Claus D", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Miller", "given" : "Stephan", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Radiology", "id" : "ITEM-2", "issue" : "1", "issued" : { "date-parts" : [ [ "2009" ] ] }, "page" : "254-63", "title" : "Ultrafast whole-body MR angiography with two-dimensional parallel imaging at 3.0 T: feasibility study.", "type" : "article-journal", "volume" : "250" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=864c5205-4bea-42c9-9edf-abd89ddb7cc4" ] } ], "mendeley" : { "formattedCitation" : "<sup><sup>5</sup></sup><sup>6</sup></sup></sup>",

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"https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }} Similar

technical success has been described at 1.5T and 3T, however 3T systems offer the benefit of a

two-fold increase in SNR and an associated fourfold increase in CNR secondary to longer T<sub>1</sub>

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significant increase in the qualitative image quality score ( $P < 0.001$ ). CONCLUSION: This study demonstrates that reducing the contrast dose at 3.0T can result in an increase in the CNR in the vessels of interest without significantly affecting the SNR.

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For the acquisition of the WB-MRA several techniques have been described including the

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"OBJECTIVE: The principal aim of the present study was to explore the feasibility of using

whole-body magnetic resonance angiography to assess atherosclerosis in different vascular

territories in a cohort of elderly. METHODS AND RESULTS: Three hundred six 70-year-old

subjects (145 women, 161 men) recruited from a population-based cohort study (Prospective

Investigation of the Vasculature in Uppsala Seniors, ie, the PIVUS study) underwent 1.5-T

whole-body magnetic resonance angiography with gadodiamide. The arteries were divided into

26 segments. In total, 7956 vessel segments were evaluated with 7900 segments (99.3%)

possible to evaluate. Of these, 7186 segments (91%) were normal. Luminal narrowing of > or =

50% was observed in 9 (1.5%) of the renal arteries, 12 (1.8%) of the carotid arteries, in 31

segments (1.1%) of the pelvic/upper leg territories, and in 136 segments (6.2%) of territories in

the lower leg. Approximately one-third of the sample had no vascular abnormalities, one-third

had stenoses of < 50%, and the remainder had stenoses > or = 50% or occlusions. Six subjects (2%) had aortic aneurysms. In subjects without evident vascular disease, 26% had significant vascular abnormalities. CONCLUSIONS: Whole-body magnetic resonance angiography performed with a clinical scanner can be used for quantifying atherosclerosis in different vascular territories in a single examination in an elderly population.", "author": [ { "dropping-particle": "", "family": "Hansen", "given": "T", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "WikstrWu00f6m", "given": "J", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Johansson", "given": "L O", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Lind", "given": "Lars", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "AhlstrWu00f6m", "given": "H", "non-dropping-particle": "", "parse-names": false, "suffix": "" } ], "container-title": "Arteriosclerosis, thrombosis, and vascular biology", "id": "ITEM-1", "issue": "3", "issued": { "date-parts": [ [ "2007", "3" ] ] }, "page": "649-54", "title": "The prevalence and quantification of atherosclerosis in an elderly population assessed by whole-body magnetic resonance angiography.", "type": "article-journal", "volume": "27" }, "uris": [ "http://www.mendeley.com/documents/?uuid=6863ba32-b8e6-411c-9c0a-403d9496992c" ] } ], "mendeley": { "formattedCitation": "<sup><sup>9</sup></sup>", "plainTextFormattedCitation": "9", "previouslyFormattedCitation":

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segments ( $r = 0.42$ ,  $p = 0.01$ ) with no correlation with the rest of the body. ABPI correlated with the whole body atheroma score ( $r = -0.39$ ,  $p = 0.012$ ), which was due to a strong correlation with the ilio-femoral vessels with no correlation with the thoracic or neck vessels. On multiple linear regression, no correlation between CIMT and global atheroma burden was present ( $r = 0.13$ ,  $p = 0.45$ ), while the correlation between ABPI and atheroma burden persisted ( $r = -0.45$ ,  $p = 0.005$ ). CONCLUSION: ABPI but not CIMT correlates with global atheroma burden as measured by whole body contrast enhanced magnetic resonance angiography in a population with symptomatic peripheral arterial disease. However this is primarily due to a strong correlation with ilio-femoral atheroma burden.", "author" : [ {

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assess image quality, presence of artifacts, arterial stenosis, and interobserver agreement of

Tim-CT in assessment of the arterial system using contrast-enhanced whole-body-MRA (CE-Wb-MRA) with a single contrast-medium injection in patients with arteriosclerosis. MATERIALS AND METHODS: The retrospective study included 18 patients (mean age, 68 years). A total of 468 arteries were evaluated. CE-Wb-MRA was performed using Tim-CT technology on a 1.5 Tesla (T) MRI after injecting a single dose of Vasovist. Evaluations were independently performed by two radiologists. The arterial system was divided into seven anatomic locations. Each radiologist assessed the image quality, degree of artifacts, and arterial stenosis in different locations. RESULTS: All Wb-MRA examinations were technically successful. Image quality: 28.42% arteries were excellent, 29.17% were good, 22.54% were satisfactory, 9.40% were poor, and 5.13% of insufficient quality. Occurrence of artifacts: 37.25% were free of artifacts, 49.44% minimal artifacts not affecting diagnosis, and 13.31% strong artifacts not permitting a diagnosis. A total of 60.00% arteries showed no stenosis, 8.76% were  $\leq 25\%$  stenotic, 5.17% were 51-75% stenotic, 4.38% were 76-99%, and 8.54% total occlusion. The interobserver agreement was good for supra-aortic, pelvic, and upper and lower leg regions. CONCLUSION: CE-Wb-MRA using the TimCT technology and with a single contrast injection is a feasible tool for whole-body MRA.

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was to determine the diagnostic performance of 3T whole-body magnetic resonance  
angiography (WB-MRA) using a hybrid protocol in comparison with a standard protocol in  
patients with peripheral arterial disease (PAD). In 26 consecutive patients with PAD two  
different protocols were used for WB-MRA: a standard sequential protocol (n = 13) and a

hybrid protocol (n = 13). WB-MRA was performed using a gradient echo sequence, body coil for signal reception, and gadoterate meglumine as contrast agent (0.3 mmol/kg body weight). Two blinded observers evaluated all WB-MRA examinations with regard to presence of stenoses, as well as diagnostic quality and degree of venous contamination in each of the four stations used in WB-MRA. Digital subtraction angiography served as the method of reference. Sensitivity for detecting significant arterial disease (luminal narrowing  $\geq$  50%) using standard-protocol WB-MRA for the two observers was 0.63 (95%CI: 0.51-0.73) and 0.66 (0.58-0.78). Specificities were 0.94 (0.91-0.97) and 0.96 (0.92-0.98), respectively. In the hybrid protocol WB-MRA sensitivities were 0.75 (0.64-0.84) and 0.70 (0.58-0.8), respectively. Specificities were 0.93 (0.88-0.96) and 0.95 (0.91-0.97). Interobserver agreement was good using both the standard and the hybrid protocol, with kappa = 0.62 (0.44-0.67) and kappa = 0.70 (0.59-0.79), respectively. WB-MRA quality scores were significantly higher in the lower leg using the hybrid protocol compared to standard protocol (p = 0.003 and p = 0.03, observers 1 and 2). Distal venous contamination scores were significantly lower with the hybrid protocol (p = 0.02 and p = 0.01, observers 1 and 2). In conclusion, hybrid-protocol WB-MRA shows a better diagnostic performance than standard protocol WB-MRA at 3 T in patients with PAD.", "author": [ { "dropping-particle": "", "family": "Nielsen", "given": "Yousef W", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Eiberg", "given": "Jonas P", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "",

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Contrast values were calculated. Qualitative evaluation: Evaluation of regions I-IV regarding vessel contrast, venous overlay and image quality on a five-point scale by two reviewers in consensus. The Mann-Whitney-U test was used to test the differences for significance. RESULTS

Quantitative evaluation: Using the double injection protocol, significantly higher contrast values in regions I and II and significantly lower contrast values in the subregions IIIa (upper part of III) and IVb (lower part of IV) were obtained ( $p < 0.05$ ). The mean contrast values in subregions IIIb (lower part of III) and IVa (upper part of IV) were lower using the double injection protocol, but not significantly. Qualitative evaluation: Using the double injection protocol, region II was rated significantly higher (mean ratings: 3.55, 3.45 and 3.5 versus 2.7, 2.5 and 2.55;  $p < 0.05$ ) and region III significantly lower (mean ratings: 3.1, 2, 2.5 versus 3.9, 3.1 and 3.55;  $p < 0.05$ ) for all three examined criteria. When using the double injection protocol, ratings were significantly lower in region IV regarding vessel contrast and image quality (mean ratings: 2.4 and 2.15 versus 3.45 and 3.15;  $p < 0.05$ ). The ratings regarding venous overlay in region IV showed no significant differences (mean ratings: 2.15 versus 2.75;  $p > 0.05$ ). CONCLUSION Due to the better results in the supraaortic/thoracic and abdominal/pelvic regions, the double injection protocol is preferred. However, both protocols require further improvement.", "author" : [ { "dropping-particle" : "", "family" : "Klessen", "given" : "C", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Asbach", "given" : "P", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" :

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Patients are imaged head first and supine without the need for manual repositioning mid-protocol. Surface coils are used to cover the entirety of the body (Figure 1). This typically requires separate head, neck, spine, two body matrices and peripheral angiography coils. This arrangement makes full utility of the maximal achievable signal-to-noise ratio (SNR) at each site maximizing spatial resolution which is essential given the 20s acquisition window for MRA.

Imaging of the whole body is acquired in 4 separate numbered stations as follows: 1) head & neck vessels extending to the level of the diaphragm, 2) abdominal vessels, 3) upper aspect of the lower limb and 4) lower aspect of the lower limb. Whole body TOF scouts are used for mapping the orientation of the vessels for planning the aforementioned stations. Once the scout sequences for the individual stations are acquired, pre-contrast mask sequences are obtained of stations 1 and 4 using a 3D gradient echo sequence. Subsequent to this, the first contrast injection is administered via a single 20G intravenous cannula sited in the antecubital fossa. Contrast is administered via a MRI compatible contrast pump injector with contrast injection volumes and rates as used in the published literature are described in Table 1.

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advantageous for the recently introduced concept of total-body magnetic resonance angiography (MRA), allowing whole-body coverage, extending from the carotid arteries to the runoff vessels, in merely 72 seconds. MATERIALS AND METHODS: Total-body three-dimensional (3D) MRA using a 1 M Gd-chelate (gadobutrol, Gadovist, Schering, Berlin, Germany) at a dosage of 0.2 mmol/kg body-weight (biphasic injection protocol: 1.3 mL/second and 0.7 mL/second) was performed on three healthy volunteers and ten consecutive patients with DSA-documented peripheral vascular disease. Separated by at least 72 hours, the three healthy volunteers also underwent the same MRA-protocol, using gadopentetate dimeglumine in equimolar dosages. RESULTS: Compared to equimolar dosages, mean signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) values in the three volunteers were significantly higher (up to 32.5% for the arteries of the thighs and calves) using gadobutrol. In the ten patients, gadobutrol-based total-body MRA accurately assessed significant stenoses (luminal narrowing > 50%) with sensitivities and specificities of 96.2% (95% CI 0.83-0.97) and 95.7% (95% CI 0.84-0.96), respectively, compared to digital subtraction angiography. CONCLUSION: The MRA image quality for total-body MRA provided by the administration of gadobutrol is superior to that obtained following administration of an identical dose of gadopentetate dimeglumine, and therefore shows promise for use as a comprehensive single exam assessing the entire arterial system for the presence of atherosclerotic disease manifestations.", "author" : [ { "dropping-particle" : "", "family" : "Goyen", "given" : "Mathias", "non-dropping-particle" : "", "parse-names"



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dimensional MR angiography: Preliminary experience", "type" : "article-journal", "volume" : "17"  
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9e2c711184dd" ] ], "mendeley" : { "formattedCitation" : "<sup><sup>14</sup></sup>",  
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style-language/schema/raw/master/csl-citation.json" }} Sagittal-oblique fluoroscopic MR

images of the thoracic aorta are used, with signal acquisition triggered when the contrast

reaches the aortic arch. Angiographic image acquisition of station 1 and then station 4 is

performed with three sets of volumetric data for station 4 obtained to optimise calf vessel

enhancement. A 10-minute delay between contrast injections is advised to allow for contrast

washout and reduce artefact from venous contamination.{ADDIN CSL\_CITATION {

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delivery rate used in a novel whole-body magnetic resonance angiography (MRA) protocol

using a 3.0T MR scanner. MATERIALS AND METHODS: Six groups of 20 consenting volunteers

underwent whole-body MRA, with each group receiving a different contrast dose and contrast

delivery rate. The arterial tree was divided into 16 segments and the image quality at each of

the anatomical locations, covering the whole body, was assessed. Qualitative analysis was

carried out using a scoring assessment of image quality, and quantitative assessments were

performed by measuring contrast-to-noise (CNR) and a signal-to-noise (SNR) index. RESULTS:

Reducing the contrast dose from 40 mL to 25 mL was found to significantly increase the CNR

in several vessels of interest in the arterial tree. There was also a significant increase in the

qualitative image quality score ( $P < 0.001$ ). CONCLUSION: This study demonstrates that

reducing the contrast dose at 3.0T can result in an increase in the CNR in the vessels of

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"<sup><sup>8</sup></sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-

style-language/schema/raw/master/csl-citation.json" }} Following this delay, the second contrast injection is administered, this time coronal oblique fluoroscopic MR images of the abdominal aorta are used to time MRA acquisition, with acquisition of station 2 triggered when contrast reaches the abdominal aorta, immediately followed by station 3. See Table 2 for typical sequence acquisition parameters. A breathhold for station 3 should be performed when the primary purpose of the exam is to evaluate the renal arteries. Adjustment for height is typically done by increasing or reducing the degree of overlap of the stations. In exceptionally tall individuals (>200cm) where the 4 stations cannot capture the entire vascular tree we would recommend excluding the cranial component, with addition of a 3D TOF sequence to compensate for the loss of this.

The whole examination including set up would usually take approximately 40 minutes. Despite the risk of the seemingly restrictive nature of the whole body coils potentiating patient claustrophobia we have found this to be highly tolerable both in healthy volunteers and patients. Locally we have performed over 1,700 scans with this technique with a <5% drop out rate due to inability to tolerate the examinations to date which is of equivalence to our routine clinical MRI.

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and cardiac MR assessment. It is accepted that there is a high disease burden in patients with diabetes, however the quantification of the whole body atheroma burden in both arterial and cardiac disease has not been previously reported. In this study we compare the quantified atheroma burden in those individuals with and without diabetes by clinical cardiovascular disease (CVD) status. METHODS 158 participants underwent WB CMR, and were categorised into one of four groups: (1) type 2 diabetes mellitus (T2DM) with CVD; (2) T2DM without CVD; (3) CVD without T2DM; (4) healthy controls. The arterial tree was subdivided into 31 segments and each scored according to the degree of stenosis. From this a standardised atheroma score (SAS) was calculated. Cardiac MR and late gadolinium enhancement images of the left ventricle were obtained for assessment of mass, volume and myocardial scar assessment. RESULTS 148 participants completed the study protocol-61 % male, with mean age of 64  $\pm$  8.2 years. SAS was highest in those with cardiovascular disease without diabetes [10.1 (0-39.5)], followed by those with T2DM and CVD [4 (0-41.1)], then those with T2DM only [3.23 (0-19.4)] with healthy controls having the lowest atheroma score [2.4 (0-19.4)]. Both groups with a prior history of CVD had a higher SAS and left ventricular mass than those without ( $p < 0.001$  for both). However after accounting for known cardiovascular risk factors, only the SAS in the group with CVD without T2DM remained significantly elevated. 6 % of the T2DM group had evidence of silent myocardial infarct, with this subcohort having a higher SAS than the remainder of the T2DM group [7.7 (4-19) vs. 2.8 (0-17),  $p = 0.024$ ]. CONCLUSIONS Global

atheroma burden was significantly higher in those with known cardiovascular disease and without diabetes but not in those with diabetes and cardiovascular disease suggesting that cardiovascular events may occur at a lower atheroma burden in diabetes.", "author" : [ { "dropping-particle" : "", "family" : "Duce", "given" : "Suzanne L.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Weir-McCall", "given" : "Jonathan R.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Gandy", "given" : "Stephen J.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Matthew", "given" : "Shona Z.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Cassidy", "given" : "Deirdre B.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "McCormick", "given" : "Lynne", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Rauchhaus", "given" : "Petra", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Looker", "given" : "Helen", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Colhoun", "given" : "Helen M.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Houston", "given" : "J. Graeme", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Cardiovascular diabetology", "id" : "ITEM-1", "issue" : "1", "issued" : { "date-parts" : [ [ "2015" ] ] }, "page" : "122", "publisher" : "BioMed

Central", "title" : "Cohort comparison study of cardiac disease and atherosclerotic burden in type 2 diabetic adults using whole body cardiovascular magnetic resonance imaging.", "type" : "article-journal", "volume" : "14" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=e5b62f72-c9d7-4479-8712-325d754f50c1" ] }, { "id" : "ITEM-2", "itemData" : { "DOI" : "10.1007/s10554-016-0842-z", "ISSN" : "15730743", "author" : [ { "dropping-particle" : "", "family" : "Weir-McCall", "given" : "Jonathan R.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "White", "given" : "Richard D.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Ramkumar", "given" : "Prasad G.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Gandy", "given" : "Stephen J.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Khan", "given" : "Faisel", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Belch", "given" : "Jill J F", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Struthers", "given" : "Allan D.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Houston", "given" : "J. Graeme", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "International Journal of Cardiovascular Imaging", "id" : "ITEM-2", "issue" : "5", "issued" : { "date-parts" : [ [ "2016" ] ] }, "page" : "1-8", "publisher" : "Springer Netherlands", "title" : "Follow-up of atheroma burden

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 "abstract" : "Introduction Arteriosclerosis (arterial stiffening) and atherosclerosis (plaque  
 formation) are pathophysiological processes afflicting the vasculature, both of which are  
 associated with future cardiovascular events. However the degree to which they overlap or  
 simply co-exist is poorly understood. The aim of the current study is to determine if these two  
 processes are significantly associated with one another.  
 Methods 1651 volunteers with no  
 clinical manifestation of cardiovascular disease and <20% 10-year cardiovascular risk  
 underwent a cardiac MRI and whole body MR angiogram as part of the TASCFORCE study.  
 Systemic arterial stiffness was measured using total arterial compliance (TAC)  $\frac{\text{ml}}{\text{mmHg}}$   
 calculated as the indexed stroke volume divided by the pulse pressure. Systemic atheroma  
 burden (AB) was calculated by scoring 30 arterial segments within the body based on the  
 degree of stenosis, summing these scores and normalising it to the number of assessable  
 segments.  
 Results 1515 (574 male, 53.8 $\pm$ 18.2 years-old) completed the study. On  
 multiple linear regression age ( $B=0.001$  (95%CI  $-0.002$  to  $0.003$ ),  
 $p=0.004$ ), heart rate ( $B=0.003$  (95%CI  $-0.003$  to  $0.009$ ),  $p<0.001$ ) and  
 blood pressure ( $B=0.008$  (95%CI  $-0.009$  to  $0.025$ ),  $p<0.001$ ) were



independently associated with TAC, while age ( $B=0.061$  (95%CI 0.04–0.08),  $p<0.001$ ), and smoking pack-year history ( $B=0.003$  (95%CI 0.005),  $p=0.022$ ) were independently associated with AB. TAC and AB demonstrated a significant correlation with each other (Spearman  $\rho=0.12$ ,  $p<0.001$ ), however on multivariable analysis accounting for age, blood pressure, sex, BMI, smoking status and cholesterol no significant association persisted ( $B=0.001$  (95%CI -0.004–0.002),  $p=0.62$ ).

**Conclusion** Systemic arteriosclerosis and atherosclerosis are separate entities with each determined by different risk factors. Future efforts in cardiovascular risk prevention should seek to address both of these

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atherosclerosis on cardiac MRI and whole body angiography: the tascforce study", "type" :
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### Future technical advances in WB-MRA acquisition

Dual-injection protocols were originally adopted to reduce the effects of venous contamination experienced with single-injection methods and to allow for more reliable arterial phase imaging due to sensitive control of bolus timing. However as MRI sequence acquisition times become shorter with parallel imaging and under-sampling a re-examination of the benefits may have to be performed. Fenchel et al.<sup>1</sup>

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station. Mean image quality scores were 3.13 +/- 1.15 (standard deviation) and 3.17 +/- 1.14 for observers 1 and 2, respectively (kappa = 0.81). Signal intensity measurements revealed mean SNR values between 36.2 +/- 8.0 and 56.2 +/- 17.7 and mean CNR values between 29.0 +/- 7.4 and 48.2 +/- 15.7. The data suggest that contrast-enhanced MR angiography with iPAT(2) is feasible for whole-body applications and allows acquisition of 3D data sets with adequate spatial resolution within short measurement times, facilitating a single injection of contrast material.

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demonstrated successful outcomes in WB-MRA with a single contrast injection and a 3T scanner in just 60s (excluding preparation and scouts) using enhanced parallel imaging techniques. Image quality was deemed to be very good with the exception of abdominal stations, raising the possibility that this technique might produce suboptimal images in larger patients. A further advance is the development of new moving table hardware, which allows for the acquisition of whole body images in a single continuous head to toe movement rather than in individual stations. The feasibility of this has been shown by Naguib et al.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1002/jmri.24182", "ISSN" : "10531807", "PMID" : "23681601", "abstract" : "PURPOSE: To assess image quality, presence of artifacts, arterial stenosis, and interobserver agreement of Tim-CT in assessment of the arterial system using contrast-enhanced whole-body-MRA (CE-Wb-MRA) with a single contrast-medium injection in patients with arteriosclerosis. MATERIALS AND METHODS: The retrospective study included 18 patients (mean age, 68 years). A total of 468 arteries were

evaluated. CE-Wb-MRA was performed using Tim-CT technology on a 1.5 Tesla (T) MRI after injecting a single dose of Vasovist. Evaluations were independently performed by two radiologists. The arterial system was divided into seven anatomic locations. Each radiologist assessed the image quality, degree of artifacts, and arterial stenosis in different locations.

RESULTS: All Wb-MRA examinations were technically successful. Image quality: 28.42% arteries were excellent, 29.17% were good, 22.54% were satisfactory, 9.40% were poor, and 5.13% of insufficient quality. Occurrence of artifacts: 37.25% were free of artifacts, 49.44% minimal artifacts not affecting diagnosis, and 13.31% strong artifacts not permitting a diagnosis. A total of 60.00% arteries showed no stenosis, 8.76% were  $\leq 25\%$  stenotic, 5.17% were 51-75% stenotic, 4.38% were 76-99%, and 8.54% total occlusion. The interobserver agreement was good for supra-aortic, pelvic, and upper and lower leg regions. CONCLUSION: CE-Wb-MRA using the TimCT technology and with a single contrast injection is a feasible tool for whole-body MRA.

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"<sup><sup>11</sup></sup>", "properties" : { }, "schema" : "https://github.com/citation-
style-language/schema/raw/master/csl-citation.json" }} who performed WB-MRA using a Tim-
CT platform at 1.5T. The total scan time was quick at around 7 minutes (inclusive of scout
sequences and planning) and the examination was completed with a single contrast injection.

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Although the overall data appears promising, only around half of the assessed vascular segments were noted to be excellent or good, with 22% being satisfactory and 15% being inadequate for analysis, which is significantly below the current bar set by dual injection protocols. With evolving protocols, this is a technique to be further explored in achieving a quickly obtained and clinically useful dataset. Similarly, an alternative avenue which holds potential for substantial benefits in the time efficiency of the procedure is the mDIXON sequence which allows partial background suppression without the need for a pre-contrast volume for subtraction.

{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1007/s00330-013-2833-y", "ISBN" : "1432-1084 (Electronic)", "PMID" : "23591617", "abstract" : "OBJECTIVE: To investigate the feasibility of subtractionless first-pass single contrast medium dose (0.1 mmol/kg) peripheral magnetic resonance angiography (MRA) at 1.5 T using two-point Dixon fat suppression and compare it with conventional subtraction MRA in terms of image quality. METHODS: Twenty-eight patients (13 male, 15 female; mean age 66 ± standard deviation, 66 ± 16 years) with known or suspected peripheral arterial disease underwent subtractionless and subtraction first-pass MRA at 1.5 T using two-point Dixon fat suppression. Results were compared with regard to vessel-to-background contrast. A phantom study was performed to assess the signal-to-noise ratio (SNR) of both MRA techniques. Two experienced observers scored subjective image quality. Agreement regarding subjective image quality was expressed



in quadratic weighted  $W_{03ba}$  values. **RESULTS:** Vessel-to-background contrast improved in all anatomical locations with the subtractionless method versus the subtraction method (all  $P < 0.001$ ). Subjective image quality was uniformly higher with the subtractionless method (all  $P < 0.03$ , except for the aorto-iliac arteries for observer 1,  $P = 0.052$ ). SNR was 15 % higher with the subtractionless method (31.9 vs 27.6). **CONCLUSION:** This study demonstrates the feasibility of subtractionless first-pass single contrast medium dose lower extremity MRA. Moreover, both objective and subjective image quality are better than with subtraction MRA. **KEY POINTS:**  $W_{2022}$  MRA is increasingly used for vascular applications.  $W_{2022}$  Dixon imaging offers an alternative to image subtraction for fat suppression.  $W_{2022}$  Subtractionless first-pass peripheral MRA is possible using two-point Dixon fat suppression.  $W_{2022}$  Subtractionless peripheral MRA is possible at 1.5 T a single contrast medium dose.  $W_{2022}$  Subtractionless first-pass peripheral MRA provides good image quality with few non-diagnostic studies.

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### Tailoring WB-MRA protocols

Given the two-stage injection/scanning protocols and the requirement of a suitable time interval between them, a dead space exists in the WB-MRA protocol that can be capitalized on

according to the underlying indication. Given that most scans are performed for atherosclerosis, one of the most frequently used is the addition of cardiac MRI with left ventricular assessment and late gadolinium enhancement sequences. Such an approach has been demonstrated to be feasible, both in the combined examination of WB-MRA and cardiac MRI including the assessment of cardiac structure, function and late gadolinium enhancement (LGE), useful for detection of scarring, and in the addition of neuro imaging for detection of prior stroke.

{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1016/j.crad.2015.02.003", "ISSN" : "1365-229X", "PMID" : "25791202", "abstract" : "AIM To evaluate a combined protocol for simultaneous cardiac MRI (CMR) and contrast-enhanced (CE) whole-body MR angiography (WB-MRA) techniques within a single examination. MATERIALS AND METHODS Asymptomatic volunteers (n = 48) with low-moderate risk of cardiovascular disease (CVD) were recruited. The protocol was divided into four sections: (1) CMR of left ventricle (LV) structure and function; (2) CE-MRA of the head, neck, and thorax followed by the distal lower limbs; (3) CMR LV late gadolinium enhancement assessment; and (4) CE-MRA of the abdomen and pelvis followed by the proximal lower limbs. Multiple observers undertook the image analysis. RESULTS For CMR, the mean ejection fraction (EF) was 67.3 ± 4.8% and mean left ventricular mass (LVM) was 100.3 ± 22.8 g. The intra-observer repeatability for EF ranged from 2.1-4.7% and from 9-12 g for LVM. Interobserver repeatability was 8.1% for EF and 19.1 g for LVM. No LV delayed myocardial enhancement was observed.

For WB-MRA, some degree of luminal narrowing or stenosis was seen at 3.6% of the vessel segments (involving n = 29 of 48 volunteers) and interobserver radiological opinion was consistent in 96.7% of 1488 vessel segments assessed. CONCLUSION Combined assessment of WB-MRA and CMR can be undertaken within a single examination on a clinical MRI system.

The associated analysis techniques are repeatable and may be suitable for larger-scale

cardiovascular MRI studies.", "author" : [ { "dropping-particle" : "", "family" : "Gandy", "given" : "S J", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lambert", "given" : "M", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Belch", "given" : "J J F", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Cavin", "given" : "I D", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Crowe", "given" : "E", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Littleford", "given" : "R", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Macfarlane", "given" : "J A", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Matthew", "given" : "S Z", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Martin", "given" : "P", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Nicholas", "given" : "R S", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "",

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1 and type 2 diabetic patients (n = 59; 31 males; 63.3 +/- 1.7 years) were examined by WB-MRA. Based on the findings in each vessel, we developed an overall score representing the patient's vascular atherosclerotic burden (MRI-score). The score's association with components of the MetS was assessed. RESULTS: The median MRI-score was 1.18 [range: 1.00-2.41] and MetS was present in 58% of the cohort (type 2 diabetics: 73%; type 1 diabetics: 26%). Age (p = 0.0002), HDL-cholesterol (p = 0.016), hypertension (p = 0.0008), nephropathy (p = 0.0093), CHD (p = 0.001) and MetS (p = 0.0011) were significantly associated with the score. Adjusted for age and sex, the score was significantly (p = 0.02) higher in diabetics with MetS (1.450 [1.328-1.572]) compared to those without MetS (1.108 [0.966-1.50]). The number of MetS components was associated with a linear increase in the MRI-score (increase in score: 0.09/MetS component;  $r^2 = 0.24$ , p = 0.038). Finally, using an established risk algorithm, we found a significant association between MRI-score and 10-year risk for CHD, fatal CHD and stroke. CONCLUSION: In this high-risk diabetic population, WB-MRA revealed large heterogeneity in the degree of systemic atherosclerosis. Presence and number of traits of the MetS are associated with the extent of atherosclerotic burden. These results support the perspective that diabetic patients are a heterogeneous population with increased but varying prevalence of atherosclerosis and risk.", "author" : [ { "dropping-particle" : "", "family" : "Findeisen", "given" : "Hannes M", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Weckbach", "given" : "Sabine", "non-dropping-particle" :

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experience combining the WB-MRI protocol with cardiac cine sequences and late gadolinium
enhancement sequences only incrementally increases examination time from a mean of 40
minutes to 51 minutes (although this does not include additional time setting up the ECG) –
See Figure 2 for the order of sequence acquisition in the combination of these. MR coronary

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angiography is another potential use of this time, which would ideally complement the remainder of the WB-MRA being the most significant vascular territory not covered with this technique. However while coronary MRA sequences are improving they are still some way off routine clinical use outside specialist centres.

{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1186/s12968-015-0205-2", "ISSN" : "1532-429X", "PMID" : "26597281", "abstract" : "BACKGROUND Coronary magnetic resonance angiography (MRA) is usually obtained with a free-breathing navigator-gated 3D acquisition. Our aim was to develop an alternative breath-hold approach that would allow the coronary arteries to be evaluated in a much shorter time and without risk of degradation by respiratory motion artifacts. For this purpose, we implemented a breath-hold, non-contrast-enhanced, quiescent-interval slice-selective (QISS) 2D technique. Sequence performance was compared at 1.5 and 3 Tesla using both radial and Cartesian k-space trajectories. METHODS The left coronary circulation was imaged in six healthy subjects and two patients with coronary artery disease. Breath-hold QISS was compared with T2-prepared 2D balanced steady-state free-precession (bSSFP) and free-breathing, navigator-gated 3D bSSFP. RESULTS Approximately 10 2.1-mm thick slices were acquired in a single ~20-s breath-hold using two-shot QISS. QISS contrast-to-noise ratio (CNR) was 1.5-fold higher at 3 Tesla than at 1.5 Tesla. Cartesian QISS provided the best coronary-to-myocardium CNR, whereas radial QISS provided the sharpest coronary images. QISS image quality exceeded that of free-breathing 3D coronary MRA with few artifacts at either field



strength. Compared with T2-prepared 2D bSSFP, multi-slice capability was not restricted by the specific absorption rate at 3 Tesla and pericardial fluid signal was better suppressed. In addition to depicting the coronary arteries, QISS could image intra-cardiac structures, pericardium, and the aortic root in arbitrary slice orientations. CONCLUSIONS Breath-hold QISS is a simple, versatile, and time-efficient method for coronary MRA that provides excellent image quality at both 1.5 and 3 Tesla. Image quality exceeded that of free-breathing, navigator-gated 3D MRA in a much shorter scan time. QISS also allowed rapid multi-slice bright-blood, diastolic phase imaging of the heart, which may have complementary value to multi-phase cine imaging. We conclude that, with further clinical validation, QISS might provide an efficient alternative to commonly used free-breathing coronary MRA techniques.", "author" :

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{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1097/RLI.0b013e31819a60d3", "ISSN" : "1536-0210", "PMID" : "19212269", "abstract" : "PURPOSE: The primary objective was to evaluate the prevalence of atherosclerotic disease, myocardial infarctions, and cerebrovascular disease in patients with long-standing diabetes using whole-body magnetic resonance imaging (WB-MRI) combined with whole-body magnetic resonance angiography (WB-MRA) and to estimate the cumulative disease burden in a new MRA-based score. MATERIALS AND METHODS: The study was approved by the ethics committee and all patients gave informed written consent. Sixty-five patients with long-standing (>10 years) diabetes mellitus without acute symptoms were

prospectively evaluated. The patients were clinically assessed and received WB-MRI/WB-MRA containing an examination of the brain, the heart, the arterial vessels (abdominal aorta, the supraaortic, renal, pelvic, and peripheral arteries), and the feet. Prevalence rates were calculated and compared with a healthy control group of 200 individuals after adjustment for age and sex by a logistic regression analysis using exact parameter estimates (Cochran-Mantel-Haenszel-statistics). Finally, an MRA based vessel score (sum of grades of all evaluated vessels divided by the number of vessels; grades range from 1, normal, to 6, complete occlusion) indicative of atherosclerotic disease burden was created for this study. This vessel score's association with clinical and biochemical parameters (age, sex, type of diabetes, diabetes duration, body mass index, blood pressure, smoking, coronary artery disease-status, retinopathy, serum creatinine, hemoglobin A1c test, low density lipoprotein-concentration, medication) was assessed with an age and sex adjusted analysis (generalized linear model). RESULTS: In the diabetic patients, we found prevalence rates of 49% for peripheral artery disease, 25% for myocardial infarction, 28% for cerebrovascular disease, and 22% for neuropathic foot disease. In all vascular beds, at least 50% of the pathologies were previously unknown. Myocardial infarction ( $P = 0.0002$ ), chronic ischemic cerebral lesions ( $P = 0.0008$ ), and atherosclerotic disease were significantly more common in diabetic than in control subjects (internal carotid artery:  $P = 0.006$ , vertebral artery:  $P = 0.009$ , intracerebral vessels:  $P = 0.02$ , superficial femoral artery:  $P = 0.006$ , anterior tibial artery:  $P = 0.01$ , posterior tibial artery:  $P = 0.02$ , fibular artery:  $P = 0.003$ ). The WB-MRI/WB-MRA-

based score showed a significant association with age ( $P = 0.0008$ ), male sex ( $P = 0.03$ ),  
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While the WBMRA provides an extensive arterial luminal assessment of stenosis and occlusion which may be attributable to atherosclerosis, other underlying arterial pathological processes such as large vessel vasculitis, dissection, or fibromuscular dysplasia (FMD) may be suggested by the patient history or site and morphology of stenoses. In such cases the WBMRA may require supplementary MR sequences to be acquired. These may include post contrast T1 imaging for wall enhancement in keeping with large vessel vasculitis, T1 and T2 imaging in cases suggestive of dissection. If FMD is suspected it is recognised that high resolution imaging with CT may be more sensitive than MRA and so WBMRA should not be used to exclude the diagnosis of FMD. In addition incidental findings of arterial pathology may also require additional imaging such as arteriovenous malformation.

### **Alternate MRI techniques**

While gadolinium based contrast agents are currently the agent of choice in contrast enhanced vascular imaging, there is a growing burden of literature supporting the use of ultra-small superparamagnetic iron oxide based contrast agents in vascular imaging.{ADDIN CSL\_CITATION

{ "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1016/j.crad.2016.03.020", "ISSN" : "1365229X", "PMID" : "27221526", "abstract" : "The practice of contrast-enhanced magnetic resonance angiography (CEMRA) has changed significantly in the span of a decade. Concerns regarding gadolinium (Gd)-associated nephrogenic systemic fibrosis in those with severely impaired renal function spurred developments in low-dose CEMRA and non-contrast MRA as well as efforts to seek alternative MR contrast agents. Originally developed for MR imaging use, ferumoxytol (an ultra-small superparamagnetic iron oxide nanoparticle), is currently approved by the US Food and Drug Administration for the treatment of iron deficiency anaemia in adults with renal disease. Since its clinical availability in 2009, there has been rising interest in the scientific and clinical use of ferumoxytol as an MR contrast agent. The unique physicochemical and pharmacokinetic properties of ferumoxytol, including its long intravascular half-life and high  $r_1$  relaxivity, support a spectrum of MRI applications beyond the scope of Gd-based contrast agents. Moreover, whereas Gd is not found in biological systems, iron is essential for normal metabolism, and nutritional iron deficiency poses major public health challenges worldwide. Once the carbohydrate shell of ferumoxytol is degraded, the elemental iron at its core is incorporated into the reticuloendothelial system. These considerations position ferumoxytol as a potential game changer in the field of CEMRA and MRI. In this paper, we aim to summarise our experience with the cardiovascular applications of ferumoxytol and provide a brief synopsis of ongoing investigations on ferumoxytol-enhanced MR

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"BACKGROUND: Exposure to gadolinium-based contrast agents (GBCA) in patients with chronic kidney disease (CKD) has been associated with the development of a potentially fatal disorder, nephrogenic systemic fibrosis (NSF). Although contrast-enhanced computed tomography (CT) is an alternative to magnetic resonance imaging (MRI), it carries the risk of radiation exposure and further reduction of residual renal function. Therefore we sought to assess the feasibility of ferumoxytol as an alternative to GBCA for contrast-enhanced MR angiography (MRA) in a pediatric cohort with CKD. Ferumoxytol is a parenteral iron supplement that contains ultrasmall superparamagnetic iron oxide (USPIO) and is a potent relaxivity agent for MRI. **METHODS:** We describe the MRI findings in ten pediatric patients who needed detailed vascular mapping. Ferumoxytol (4 mg/kg) was administered intravenously for contrast-enhanced MRA. The patients tolerated the procedure without complications. **RESULTS:** Resulting studies were highly diagnostic and were pivotal in guiding patient management. The images were notable for clear delineation of multiple vascular occlusions. **CONCLUSIONS:** Given the concerns associated with the use of GBCAs in renal failure, ferumoxytol is an excellent alternative contrast agent in pediatric end stage renal disease (ESRD) patients. Future studies are needed in order to further evaluate safety and efficacy of ferumoxytol in this patient population.",

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holds significant potential for whole body angiography where its vascular steady state can be capitalized on to improve spatial resolution and image quality compared to first pass image acquisition.

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"RATIONALE AND OBJECTIVES This work aimed to quantify the differences in signal-to-noise ratio (SNR) and vessel sharpness between steady-state and first-pass magnetic resonance

angiography (MRA) with ferumoxytol in renal transplant recipients. MATERIALS AND METHODS

We performed a retrospective study of adult patients who underwent steady-state and first-pass MRA with ferumoxytol to evaluate renal transplant vasculature. SNR was calculated in the external iliac artery, and vessel sharpness was calculated in the external iliac and renal

transplant arteries for both acquisitions. Data were compared using Student's t test. RESULTS

Fifteen patients were included (mean age 56.9 years, 10 males). The mean SNR of the external iliac artery was 42.2 (SD, 11.9) for the first-pass MRA and 41.8 (SD, 9.7) for the steady-state

MRA ( $p = 0.92$ ). The mean vessel sharpness was significantly higher for the steady-state MRA compared to first-pass MRA for both external iliac (1.24 vs. 0.80 mm<sup>-1</sup>,  $p < 0.01$ ) and renal

transplant arteries (1.26 vs. 0.79 mm<sup>-1</sup>,  $p < 0.01$ ). CONCLUSION Steady-state MRA using

ferumoxytol improves vessel sharpness while maintaining equivalent SNR compared to

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Venous access can often be challenging - particularly in those with chronic diseases - in addition to which those with severe chronic kidney disease are at risk of nephrogenic systemic fibrosis (NSF) secondary to gadolinium-based agents. While MRA provides excellent luminal assessment, it does not provide any information on the plaque causing the stenosis, and can miss non-stenotic atheroma with positive vessel remodelling. Non-contrast techniques which obviate the need for cannulation and/or provide arterial wall assessment are thus an attractive option.

A multitude of non-contrast protocols are currently used in clinical practice for regional MR angiography, some of which have been available for decades with others being only more recently pioneered. These include Time-of-Flight (TOF), Phase contrast (PC), Black blood (BB), ECG-gated fast-spin echo, bSSFP (balanced Steady State Free Precession), bSSFP with arterial spin labeling and QUISS (quiescent interval steady state) sequences. Each has its respective strengths and weaknesses and numerous studies have been published comparing these to contrast enhanced MRA, the examination of which is beyond the scope of this article. To date none of these have been used to obtain a non contrast WB-MRA, although in a healthy volunteer the feasibility of combining multiple different non-contrast sequences tailored to each of the arterial territories in the body has shown to be feasible.

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on two main applications: peripheral run-off and renal MRA. Recently, both applications have achieved remarkable advancements and have become a viable clinical option as an alternative to contrast-enhanced (CE)-MRA. In addition, developments on the horizon including whole body MRA applications and further advancement at 3 Tesla are discussed.

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This will no doubt continue to be an exciting area of development in years to come.

## Analysis and quantification of vascular disease

Reporting of WB-MRA images is not any different to the reporting of routinely performed regional MRA. The increased coverage does however increase the chance of incidental findings, which are particularly frequent in the cohort typically seen for WB-MRA assessment (see Figure 3). However to simply report the location and severity of stenosis, while clinically useful, potentially overlooks the additional information such a systemic assessment brings.

There are several scoring systems that attempt to address this issue. While each is distinct and separate from one another, they all contain the same key themes: the scoring of the major arteries according to the maximum degree of stenosis in each, followed by the summation of these results. The most published of these is the 'Standardised atheroma score' as described by Weir-McCall et al. (see Figure 4).

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 "<sup><sup>16</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-  
 style-language/schema/raw/master/csl-citation.json" }} In this technique the vascular system is  
 split into 31 vessels, with each scored following a 5 point scoring system based on the maximal  
 luminal stenosis: 0= Normal vessel; 1= <50% stenosis; 2= 50-70% stenosis; 3= >70% stenosis;  
 and 4= Completely occluded vessel. Such scores have been shown to be highly reproducible in  
 both those with and without known cardiovascular disease, and to correlate highly with  
 cardiovascular risk factors.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1",  
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"abstract" : "AIM To evaluate a combined protocol for simultaneous cardiac MRI (CMR) and contrast-enhanced (CE) whole-body MR angiography (WB-MRA) techniques within a single examination. MATERIALS AND METHODS Asymptomatic volunteers (n = 48) with low-moderate risk of cardiovascular disease (CVD) were recruited. The protocol was divided into four sections: (1) CMR of left ventricle (LV) structure and function; (2) CE-MRA of the head, neck, and thorax followed by the distal lower limbs; (3) CMR LV  $\text{late gadolinium enhancement}$  assessment; and (4) CE-MRA of the abdomen and pelvis followed by the proximal lower limbs. Multiple observers undertook the image analysis. RESULTS For CMR, the mean ejection fraction (EF) was  $67.3 \pm 4.8\%$  and mean left ventricular mass (LVM) was  $100.3 \pm 22.8$  g. The intra-observer repeatability for EF ranged from 2.1-4.7% and from 9-12 g for LVM. Interobserver repeatability was 8.1% for EF and 19.1 g for LVM. No LV delayed myocardial enhancement was observed. For WB-MRA, some degree of luminal narrowing or stenosis was seen at 3.6% of the vessel segments (involving n = 29 of 48 volunteers) and interobserver radiological opinion was consistent in 96.7% of 1488 vessel segments assessed. CONCLUSION Combined assessment of WB-MRA and CMR can be undertaken within a single examination on a clinical MRI system.

The associated analysis techniques are repeatable and may be suitable for larger-scale

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scoring system for whole-body magnetic resonance angiography (WBMRA) that allows  
estimation of atherosclerotic induced luminal narrowing, and determine whether the traditional  
cardiovascular (CV) risk factors included in the Framingham risk score (FRS) were related to this  
total atherosclerotic score (TAS) in an elderly population. A group of 306 subjects, aged 70,  
were recruited from the general population and underwent WBMRA in a 1.5-T scanner. Three-  
dimensional sequences were acquired after administration of one i.v. injection of 40 ml  
gadodiamide. The arterial tree was divided into five territories (carotid, aorta, renal, upper and  
lower leg) comprising 26 vessel segments, and assessed according to its degree of stenosis or  
occlusion. FRS correlated to TAS ( $r = 0.30$ ,  $P < 0.0001$ ), as well as to the atherosclerotic score  
for the five individual territories. Of the parameters included in the FRS, male gender ( $P <$   
 $0.0001$ ), systolic blood pressure ( $P = 0.0002$ ), cigarette pack-years ( $P = 0.0008$ ) and HDL  
cholesterol ( $P = 0.008$ ) contributed to the significance. A scoring system for WBMRA was  
created. The significant relation towards traditional CV risk factors indicates that the proposed  
scoring system could be of value for assessing atherosclerotically induced luminal narrowing.",

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Regardless of the precise formula used, the prognostic power of this summative data has been well established in several studies. Lundberg et al. demonstrated that the atheroma burden better predicted major adverse cardiovascular events than traditional risk scores, carotid intima

media thickness or ankle-brachial pressure index in 305 seventy year olds.{ADDIN

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"OBJECTIVE: The purpose of the present study was to investigate the relationship between the

Total Atherosclerotic Score (TAS), a measurement of the overall atherosclerotic burden of the

arterial tree by whole body magnetic resonance angiography (WBMRA), and the risk of major

adverse cardiovascular events (MACE), defined as cardiac death, myocardial infarction, stroke

and/or coronary revascularization, assuming that TAS predicts MACE. METHODS AND RESULTS:

305 randomly selected 70 year-old subjects (47% women) underwent WBMRA. Their

atherosclerotic burden was evaluated and TAS > 0, that is atherosclerotic changes, were found

in 68% of subjects. During follow-up (mean 4.8 years), MACE occurred in 25 subjects (8.2%).

Adjusting for multiple risk factors, TAS was associated with MACE (OR 8.86 for any degree of

vessel lumen abnormality, 95%CI 1.14-69.11, p = 0.037). In addition, TAS improved

discrimination and reclassification when added to the Framingham risk score (FRS), and ROC

(Receiver Operator Curve) increased from 0.681 to 0.750 (p = 0.0421). CONCLUSION: In a

population-based sample of 70 year old men and women WBMRA, with TAS, predicted MACE

independently of major cardiovascular risk factors.", "author" : [ { "dropping-particle" : "",

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style-language/schema/raw/master/csl-citation.json" }} Bamberg et al. showed similar findings  
in a diabetic cohort with the atheroma score predictive of both single and recurrent  
cardiovascular events.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : {  
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"Purpose To study the predictive value of whole-body magnetic resonance (MR) imaging for

the occurrence of cardiac and cerebrovascular events in a cohort of patients with diabetes mellitus (DM). **Materials and Methods** This HIPAA-compliant study was approved by the institutional review board. Informed consent was obtained from all patients before enrollment into the study. The authors followed up 65 patients with DM (types 1 and 2) who underwent a comprehensive, contrast material-enhanced whole-body MR imaging protocol, including brain, cardiac, and vascular sequences at baseline. Follow-up was performed by phone interview. The primary endpoint was a major adverse cardiac and cerebrovascular event (MACCE), which was defined as composite cardiac-cerebrovascular death, myocardial infarction, cerebrovascular event, or revascularization. MR images were assessed for the presence of systemic atherosclerotic vessel changes, white matter lesions, and myocardial changes. Kaplan-Meier survival and Cox regression analyses were performed to determine associations. **Results** Follow-up was completed in 61 patients (94%; median age, 67.5 years; 30 women [49%]; median follow-up, 70 months); 14 of the 61 patients (23%) experienced MACCE. Although normal whole-body MR imaging excluded MACCE during the follow-up period (0%; 95% confidence interval [CI]: 0%, 17%), any detectable ischemic and/or atherosclerotic changes at whole-body MR imaging (prevalence, 66%) conferred a cumulative event rate of 20% at 3 years and 35% at 6 years. Whole-body MR imaging summary estimate of disease was strongly predictive for MACCE (one increment of vessel score and each territory with atherosclerotic changes: hazard ratio, 13.2 [95% CI: 4.5, 40.1] and 3.9 [95% CI: 2.2, 7.5], respectively), also beyond clinical



characteristics as well as individual cardiac or cerebrovascular MR findings. Conclusion These initial data indicate that disease burden as assessed with whole-body MR imaging confers strong prognostic information in patients with DM. Wu00a9 RSNA, 2013 Online supplemental material is available for this article.", "author" : [ { "dropping-particle" : "", "family" : "Bamberg", "given" : "Fabian", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Parhofer", "given" : "Klaus G", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lochner", "given" : "Elena", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Marcus", "given" : "Roy P", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Theisen", "given" : "Daniel", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Findeisen", "given" : "Hannes M", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Hoffmann", "given" : "Udo", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "SchWu00f6nberg", "given" : "Stefan O", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Schlett", "given" : "Christopher L", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Reiser", "given" : "Maximilian F", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Weckbach", "given" : "Sabine", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ]

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(hazard rate ratio = 12.29,  $p < 0.0001$ ) remained independently associated. Assessing organ system risk, cardiac and cerebral MR findings predicted more strongly events in their respective organ system. Vessel-score predicted both cardiac and cerebral, but not non-cardiocerebral, events. CONCLUSION Whole-body MR findings predict occurrence of recurrent events in diabetics independent of clinical characteristics, and may concurrently provide organ system-specific risk. KEY POINTS Wu2022 Patients with long-standing diabetes mellitus are at high risk for recurrent events. Wu2022 Whole-body MRI predicts occurrence of recurrent events independently of clinical characteristics. Wu2022 The vessel score derived from whole-body angiography is a good general risk-marker. Wu2022 Whole-body MRI may also provide organ-specific risk assessment. Wu2022 Current findings may indicate benefits of whole-body MRI for risk stratification.", "author" : [ { "dropping-particle" : "", "family" : "Bertheau", "given" : "Robert C.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Bamberg", "given" : "Fabian", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lochner", "given" : "Elena", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Findeisen", "given" : "Hannes M.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Parhofer", "given" : "Klaus G.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Kauczor", "given" : "Hans-Ulrich", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-

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 vessel analysis, evidence of prior stroke on cranial MRI, or the presence of ventricular systolic  
 dysfunction or late gadolinium enhancement on cardiac MRI, demonstrating the prognostic  
 strength of a systematic vascular assessment. These findings have also been replicated in a  
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unanswered questions with further work required to determine what the best scoring system is,

what its implications are in those of low-intermediate cardiovascular risk, and how best to use

this data to better tailor and guide intervention in a manner which improves patient related

outcomes.

## **Clinical Applications:**

### Atherosclerosis

That arterial disease does not occur in isolation has been widely accepted in the literature for

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between arterial disease in different sites. A study of the aorta and coronary, carotid, and iliac

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"<sup><sup>1</sup></sup>" }, "properties": { }, "schema": "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }}. Having intermittent claudication as a

marker of arterial disease confers a risk of cardiac death of up to three or four times more

than those without, while cardiac death accounts for up to 75% of deaths in these

patients.{ADDIN CSL\_CITATION { "citationItems": [ { "id": "ITEM-1", "itemData": { "author": [ {

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"https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }} Multi-site

cardiovascular disease further portends a poor outcome, being a stronger independent

predictor of mortality than recent cardiovascular events.{ADDIN CSL\_CITATION { "citationItems"

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identifying which patients are highest risk for cardiovascular events. Prior ischemic events,

polyvascular disease, and diabetes mellitus have all been identified as predictors of ischemic



events, but their comparative contributions to future risk remain unclear. OBJECTIVE: To categorize the risk of cardiovascular events in stable outpatients with various initial manifestations of atherothrombosis using simple clinical descriptors. DESIGN, SETTING, AND PATIENTS: Outpatients with coronary artery disease, cerebrovascular disease, or peripheral arterial disease or with multiple risk factors for atherothrombosis were enrolled in the global Reduction of Atherothrombosis for Continued Health (REACH) Registry and were followed up for as long as 4 years. Patients from 3647 centers in 29 countries were enrolled between 2003 and 2004 and followed up until 2008. Final database lock was in April 2009. MAIN OUTCOME MEASURES: Rates of cardiovascular death, myocardial infarction, and stroke. RESULTS: A total of 45,227 patients with baseline data were included in this 4-year analysis. During the follow-up period, a total of 5481 patients experienced at least 1 event, including 2315 with cardiovascular death, 1228 with myocardial infarction, 1898 with stroke, and 40 with both a myocardial infarction and stroke on the same day. Among patients with atherothrombosis, those with a prior history of ischemic events at baseline (n = 21,890) had the highest rate of subsequent ischemic events (18.3%; 95% confidence interval [CI], 17.4%-19.1%); patients with stable coronary, cerebrovascular, or peripheral artery disease (n = 15,264) had a lower risk (12.2%; 95% CI, 11.4%-12.9%); and patients without established atherothrombosis but with risk factors only (n = 8073) had the lowest risk (9.1%; 95% CI, 8.3%-9.9%) (P < .001 for all comparisons). In addition, in multivariable modeling, the presence of diabetes (hazard ratio

[HR], 1.44; 95% CI, 1.36-1.53; P < .001), an ischemic event in the previous year (HR, 1.71; 95% CI, 1.57-1.85; P < .001), and polyvascular disease (HR, 1.99; 95% CI, 1.78-2.24; P < .001) each were associated with a significantly higher risk of the primary end point. CONCLUSION: Clinical descriptors can assist clinicians in identifying high-risk patients within the broad range of risk for outpatients with atherothrombosis.

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"<sup><sup>36</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-

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times, been attempts to utilize surrogate markers to predict the likelihood of significant morbidity with the intention of gaining this knowledge to reduce risk of cardiovascular disease by instigating preventative measures. However, scoring mechanisms based on clinical variates largely employs probability of the effect of the risk factors. Scoring systems such as the Framingham risk score have been shown to significantly overestimate risk in higher risk individuals.

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(36.3% observed vs. 44.1% expected). The c-statistic increased from 0.66 to 0.69 after refitting.

Separately estimating CHD and stroke revealed considerable heterogeneity with regard to the

contribution of CHD and stroke to total CVD risk. Conclusions Framingham CVD risk

predictions perform well in the low- to intermediate risk categories in the Rotterdam Study.

Disentangling CVD into CHD and stroke separately provides additional information about the

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The ability of WB-MRA to detect and quantify atherosclerotic burden has been well evidenced in both symptomatic and asymptomatic cohorts. Laible et al.{ADDIN CSL\_CITATION {

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resonance imaging and angiography. METHODS: A cohort of 138 individuals (118 men, 20 women) with a mean age of 54 years (SD 7.55) was referred to whole-body MRI at 1.5-T, including contrast-enhanced whole-body MR angiography (MRA) and cardiac MRI. A total of 2,065/2,070 vessel segments (99.8%) and cardiac function were evaluated. RESULTS: Approximately one-fourth of the participating individuals had vascular abnormalities. In 17 subjects (12.3% of all subjects) significant luminal narrowing was observed in at least one vascular segment. Luminal narrowing (mild to severe) was observed in 1 (0.7% of all subjects respectively) of the renal arteries, 7 (5.0%) of the carotid arteries, and 3 (2.2%) of the pelvic and upper leg arteries, and in 17 segments (12.3%) of arteries in the lower leg. In cardiac function and perfusion imaging, wall motion disorders were observed in six patients (4.3%), with additional delayed enhancement and isolated delayed enhancement present in two cases. Functional parameters differed from reference values in 55 cases. CONCLUSIONS: Even in an asymptomatic cohort of middle-aged predominantly male individuals, atherosclerotic disease is not uncommon and is detectable by whole-body MRI. MAIN MESSAGES: In middle-aged predominantly male individuals, atherosclerotic disease is not uncommon. Even in an asymptomatic collective, approximately one fourth had vascular abnormalities. Using whole-body MR angiography (MRA), 99.8% of 2,070 vessel segments could be evaluated.", "author" : [ { "dropping-particle" : "", "family" : "Laible", "given" : "M", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" :

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was present in 27% of a cohort of one hundred and thirty-eight individuals free from cardiovascular disease. Weckback *et al.*{ADDIN CSL\_CITATION { "citationItems": [ { "id": "ITEM-1", "itemData": { "DOI": "10.1097/RLI.0b013e31819a60d3", "ISSN": "1536-0210", "PMID": "19212269", "abstract": "PURPOSE: The primary objective was to evaluate the prevalence of atherosclerotic disease, myocardial infarctions, and cerebrovascular disease in patients with long-standing diabetes using whole-body magnetic resonance imaging (WB-MRI) combined with whole-body magnetic resonance angiography (WB-MRA) and to estimate the cumulative disease burden in a new MRA-based score. MATERIALS AND METHODS: The study was approved by the ethics committee and all patients gave informed written consent. Sixty-five patients with long-standing (>10 years) diabetes mellitus without acute symptoms were prospectively evaluated. The patients were clinically assessed and received WB-MRI/WB-MRA containing an examination of the brain, the heart, the arterial vessels (abdominal aorta, the supraaortic, renal, pelvic, and peripheral arteries), and the feet. Prevalence rates were calculated and compared with a healthy control group of 200 individuals after adjustment for age and sex by a logistic regression analysis using exact parameter estimates (Cochran-Mantel-Haenszel-statistics). Finally, an MRA based vessel score (sum of grades of all evaluated vessels divided by the number of vessels; grades range from 1, normal, to 6, complete occlusion) indicative of atherosclerotic disease burden was created for this study. This vessel score's association with clinical and biochemical parameters (age, sex, type of diabetes, diabetes duration, body mass

index, blood pressure, smoking, coronary artery disease-status, retinopathy, serum creatinine, hemoglobin A1c test, low density lipoprotein-concentration, medication) was assessed with an age and sex adjusted analysis (generalized linear model). RESULTS: In the diabetic patients, we found prevalence rates of 49% for peripheral artery disease, 25% for myocardial infarction, 28% for cerebrovascular disease, and 22% for neuropathic foot disease. In all vascular beds, at least 50% of the pathologies were previously unknown. Myocardial infarction ( $P = 0.0002$ ), chronic ischemic cerebral lesions ( $P = 0.0008$ ), and atherosclerotic disease were significantly more common in diabetic than in control subjects (internal carotid artery:  $P = 0.006$ , vertebral artery:  $P = 0.009$ , intracerebral vessels:  $P = 0.02$ , superficial femoral artery:  $P = 0.006$ , anterior tibial artery:  $P = 0.01$ , posterior tibial artery:  $P = 0.02$ , fibular artery:  $P = 0.003$ ). The WB-MRI/WB-MRA-based score showed a significant association with age ( $P = 0.0008$ ), male sex ( $P = 0.03$ ), nephropathy ( $P = 0.026$ ), "author": [ { "dropping-particle": "", "family": "Weckbach", "given": "Sabine", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Findeisen", "given": "Hannes M", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Schoenberg", "given": "Stefan O", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Kramer", "given": "Harald", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Stark", "given": "Renee", "non-dropping-particle": "", "parse-names": false, "suffix": "" }, { "dropping-particle": "", "family": "Clevert", "given": "Dirk A",

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 "<sup><sup>22</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-  
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 occult atherosclerotic disease in a prospective case-control population of 65 well-treated  
 longstanding diabetic patients, with 57% demonstrating at least one vessel with >50% stenosis,  
 and with 50% of these lesions detected on WB-MRA not previously known about. In those  
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 stenosis) in 37-55% of those with coronary artery disease {ADDIN CSL\_CITATION {  
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strongest independent predictor for CAD with a 11-fold increase in likelihood to suffer from significant coronary disease. On the contrary, while 15/27 (55%) of patients with CAD exhibited at least one extra-cardiac stenosis > 50%, only 3/22 (14%) of those patients without CAD did (p = 0.003). The likelihood for an extra-cardiac stenosis when CAD is present differed between vascular territories and ranged from 15% for a carotid stenosis to 44% for a stenosis in the lower extremities. CONCLUSION: This study provides important new evidence for the close association of extra-cardiac and coronary atherosclerosis. The novel findings that a WB-MRA derived systemic atherosclerosis score index is not only associated with established cardiovascular risk scores but is also predictive of significant CAD suggest its potential prognostic implications and underline the importance to screen for coronary disease in patients with extra-cardiac manifestations of atherosclerosis.", "author" : [ { "dropping-particle" : "", "family" : "Lehrke", "given" : "Stephanie", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Egenlauf", "given" : "Benjamin", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Steen", "given" : "Henning", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lossnitzer", "given" : "Dirk", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Korosoglou", "given" : "Grigorius", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Merten", "given" : "Constanze", "non-dropping-particle" : "", "parse-

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aortic aneurysms (AAA) (five segments). Of the 73 segments, 36 were deemed necessary for further investigation by means of focused MRA examinations; the diagnosis was confirmed in all cases. Within the 60-day follow-up period, interventional or surgical therapy outside the peripheral arterial tree was performed in nine patients (11 segments), including carotid endarterectomy and renal artery angioplasty. The outlined total-body 3D MRA approach permits a comprehensive evaluation of the arterial system in patients with atherosclerosis and does indeed have an impact on patient management in patients with PAOD."

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The inclusion of cardiac assessment into the WB-MRA protocol reveals further hidden disease, with silent myocardial infarcts reported in 29% of those with PAD, 14% of those with diabetes and up to 20% of healthy 70 year olds.

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identifies myocardial scars and thereby has the potential to detect UMI. METHODS: Cardiac MRI was performed on 259 randomly chosen 70-year-old subjects. Late enhancement and cine sequences were acquired, and the ejection fraction and left ventricular (LV) mass were calculated. Late enhancement involving the subendocardial layer was considered to represent myocardial infarction (MI) scars, and their volumes were calculated. Information on cardiac morbidity and risk factors was collected from medical records and from a health examination. Subjects with MI scars, with or without a hospital diagnosis of MI were classified as RMI or UMI, respectively. RESULTS: The images from 248 subjects (123 women, 125 men) were assessable. Myocardial infarction scars were found in 60 subjects (24.2%), in 49 of whom (19.8%) they were UMIs. The volumes of the UMIs were significantly smaller than those of the RMIs. There was an increased frequency of chest pain symptoms among the subjects with UMI or RMI compared with those without MI scars. Ejection fraction was significantly lower and LV mass significantly larger in the subjects with UMI or RMI than in those without MI scars. CONCLUSIONS: Unrecognized MI detected with MRI was more frequent than expected in 70-year-old subjects. The subjects displaying these UMIs may represent a previously unknown potential risk group for future cardiovascular events.", "author" : [ { "dropping-particle" : "", "family" : "Barbier", "given" : "Charlotte Ebeling", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Bjerner", "given" : "Tomas", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" :



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prevalence of atherosclerotic disease, myocardial infarctions, and cerebrovascular disease in  
patients with long-standing diabetes using whole-body magnetic resonance imaging (WB-MRI)  
combined with whole-body magnetic resonance angiography (WB-MRA) and to estimate the  
cumulative disease burden in a new MRA-based score. MATERIALS AND METHODS: The study  
was approved by the ethics committee and all patients gave informed written consent. Sixty-  
five patients with long-standing (>10 years) diabetes mellitus without acute symptoms were  
prospectively evaluated. The patients were clinically assessed and received WB-MRI/WB-MRA  
containing an examination of the brain, the heart, the arterial vessels (abdominal aorta, the

supraaortic, renal, pelvic, and peripheral arteries), and the feet. Prevalence rates were calculated and compared with a healthy control group of 200 individuals after adjustment for age and sex by a logistic regression analysis using exact parameter estimates (Cochran-Mantel-Haenszel-statistics). Finally, an MRA based vessel score (sum of grades of all evaluated vessels divided by the number of vessels; grades range from 1, normal, to 6, complete occlusion) indicative of atherosclerotic disease burden was created for this study. This vessel score's association with clinical and biochemical parameters (age, sex, type of diabetes, diabetes duration, body mass index, blood pressure, smoking, coronary artery disease-status, retinopathy, serum creatinine, hemoglobin A1c test, low density lipoprotein-concentration, medication) was assessed with an age and sex adjusted analysis (generalized linear model). RESULTS: In the diabetic patients, we found prevalence rates of 49% for peripheral artery disease, 25% for myocardial infarction, 28% for cerebrovascular disease, and 22% for neuropathic foot disease. In all vascular beds, at least 50% of the pathologies were previously unknown. Myocardial infarction ( $P = 0.0002$ ), chronic ischemic cerebral lesions ( $P = 0.0008$ ), and atherosclerotic disease were significantly more common in diabetic than in control subjects (internal carotid artery:  $P = 0.006$ , vertebral artery:  $P = 0.009$ , intracerebral vessels:  $P = 0.02$ , superficial femoral artery:  $P = 0.006$ , anterior tibial artery:  $P = 0.01$ , posterior tibial artery:  $P = 0.02$ , fibular artery:  $P = 0.003$ ). The WB-MRI/WB-MRA-based score showed a significant association with age ( $P = 0.0008$ ), male sex ( $P = 0.03$ ), nephropathy ( $P = 0.0026$ ), "author" : [ { "dropping-particle" : "", "family" : "Weckbach", "given" :

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The impact of the atheroma burden in terms of prognosis is significant. In a study of 305 seventy year olds the presence of atherosclerosis on WB-MRA was associated with an odds ratio of 8.86 for a major adverse cardiovascular event compared to those with a normal study after adjusting for sex, waist circumference, body mass index, fasting blood glucose, systolic blood pressure, HDL and LDL-cholesterol, serum triglycerides, smoking and hsC-reactive protein.

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vessel lumen abnormality, 95%CI 1.14-69.11,  $p = 0.037$ ). In addition, TAS improved discrimination and reclassification when added to the Framingham risk score (FRS), and ROC (Receiver Operator Curve) increased from 0.681 to 0.750 ( $p = 0.0421$ ). CONCLUSION: In a population-based sample of 70 year old men and women WBMRA, with TAS, predicted MACE independently of major cardiovascular risk factors.", "author" : [ { "dropping-particle" : "", "family" : "Lundberg", "given" : "Christina", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Johansson", "given" : "Lars", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Barbier", "given" : "Charlotte Ebeling", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lind", "given" : "Lars", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Ahlstr  m", "given" : "H  kan", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Hansen", "given" : "Tomas", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Atherosclerosis", "id" : "ITEM-1", "issue" : "1", "issued" : { "date-parts" : [ [ "2013", "5" ] ] }, "page" : "148-52", "title" : "Total atherosclerotic burden by whole body magnetic resonance angiography predicts major adverse cardiovascular events.", "type" : "article-journal", "volume" : "228" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=d16a0da1-74b8-4b50-9bdf-7ac5a37824f2" ] } ], "mendeley" : { "formattedCitation" : "<sup><sup>29</sup></sup>",

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In another study by Bamburg et al. those with a normal WB-MRA had no cardiovascular events at 6 years, and in those who did have evidence of atherosclerosis, each point increase in atheroma score was associated with a hazard ratio of 13.2 for major adverse cardiovascular events.

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whole-body magnetic resonance (MR) imaging for the occurrence of cardiac and

cerebrovascular events in a cohort of patients with diabetes mellitus (DM). Materials and  
Methods This HIPAA-compliant study was approved by the institutional review board. Informed  
consent was obtained from all patients before enrollment into the study. The authors followed  
up 65 patients with DM (types 1 and 2) who underwent a comprehensive, contrast material-  
enhanced whole-body MR imaging protocol, including brain, cardiac, and vascular sequences  
at baseline. Follow-up was performed by phone interview. The primary endpoint was a major  
adverse cardiac and cerebrovascular event (MACCE), which was defined as composite cardiac-  
cerebrovascular death, myocardial infarction, cerebrovascular event, or revascularization. MR  
images were assessed for the presence of systemic atherosclerotic vessel changes, white matter  
lesions, and myocardial changes. Kaplan-Meier survival and Cox regression analyses were

performed to determine associations. Results Follow-up was completed in 61 patients (94%; median age, 67.5 years; 30 women [49%]; median follow-up, 70 months); 14 of the 61 patients (23%) experienced MACCE. Although normal whole-body MR imaging excluded MACCE during the follow-up period (0%; 95% confidence interval [CI]: 0%, 17%), any detectable ischemic and/or atherosclerotic changes at whole-body MR imaging (prevalence, 66%) conferred a cumulative event rate of 20% at 3 years and 35% at 6 years. Whole-body MR imaging summary estimate of disease was strongly predictive for MACCE (one increment of vessel score and each territory with atherosclerotic changes: hazard ratio, 13.2 [95% CI: 4.5, 40.1] and 3.9 [95% CI: 2.2, 7.5], respectively), also beyond clinical characteristics as well as individual cardiac or cerebrovascular MR findings. Conclusion These initial data indicate that disease burden as assessed with whole-body MR imaging confers strong prognostic information in patients with DM.

Wu00a9 RSNA, 2013 Online supplemental material is available for this article.", "author" : [ { "dropping-particle" : "", "family" : "Bamberg", "given" : "Fabian", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Parhofer", "given" : "Klaus G", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Lochner", "given" : "Elena", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Marcus", "given" : "Roy P", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Theisen", "given" : "Daniel", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-

particle" : "", "family" : "Findeisen", "given" : "Hannes M", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Hoffmann", "given" : "Udo", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "SchWu00f6nberg", "given" : "Stefan O", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Schlett", "given" : "Christopher L", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Reiser", "given" : "Maximilian F", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Weckbach", "given" : "Sabine", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Radiology", "id" : "ITEM-1", "issue" : "3", "issued" : { "date-parts" : [ [ "2013", "12" ] ] }, "page" : "730-7", "title" : "Diabetes Mellitus: Long-term Prognostic Value of Whole-Body MR Imaging for the Occurrence of Cardiac and Cerebrovascular Events.", "type" : "article-journal", "volume" : "269" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=ab2f7f9b-613e-4f38-8092-bbb9edbfa2b0" ] } ], "mendeley" : { "formattedCitation" : "<sup><sup>30</sup></sup>", "plainTextFormattedCitation" : "30", "previouslyFormattedCitation" : "<sup><sup>30</sup></sup>", "properties" : { }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" } } Inclusion of a WB-MRA derived atheroma score yielded a 0.32 improvement in net reclassification of risk, with an increase in the C-statistic ROC (Receiver Operator Curve) from 0.681 for the Framingham risk score alone,



to 0.750 for the Framingham risk score and atheroma score combined.

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"ISSN" : "1879-1484", "PMID" : "23474127", "abstract" : "OBJECTIVE: The purpose of the present  
study was to investigate the relationship between the Total Atherosclerotic Score (TAS), a  
measurement of the overall atherosclerotic burden of the arterial tree by whole body magnetic  
resonance angiography (WBMRA), and the risk of major adverse cardiovascular events (MACE),  
defined as cardiac death, myocardial infarction, stroke and/or coronary revascularization,  
assuming that TAS predicts MACE. METHODS AND RESULTS: 305 randomly selected 70 year-  
old subjects (47% women) underwent WBMRA. Their atherosclerotic burden was evaluated and  
TAS > 0, that is atherosclerotic changes, were found in 68% of subjects. During follow-up  
(mean 4.8 years), MACE occurred in 25 subjects (8.2%). Adjusting for multiple risk factors, TAS  
was associated with MACE (OR 8.86 for any degree of vessel lumen abnormality, 95%CI 1.14-  
69.11, p = 0.037). In addition, TAS improved discrimination and reclassification when added to  
the Framingham risk score (FRS), and ROC (Receiver Operator Curve) increased from 0.681 to  
0.750 (p = 0.0421). CONCLUSION: In a population-based sample of 70 year old men and  
women WBMRA, with TAS, predicted MACE independently of major cardiovascular risk  
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"1936878X", "PMID" : "23582355", "abstract" : "Objectives: The aim of the study was to

determine the association of coronary computed tomographic angiography (CTA)-identified

coronary artery disease (CAD) with post-test aspirin, statin, and antihypertensive medication

use and changes in cholesterol and blood pressure (BP). Background: The relationship of CTA

findings to subsequent changes in preventive cardiovascular medication prescribing patterns

and risk factors is largely unknown. Methods: We studied 1,125 consecutive patients without

known CAD referred for coronary CTA. CAD was defined as none, nonobstructive (<50%), or

obstructive (≥50%). Prescriptions were queried in the 6 months pre- and post-CTA for

comparison of aspirin, statin, and BP treatment. Medication intensification was defined as

initiation, dose increase, or, for statins, change to a more potent formulation. Lipid and BP

values were obtained at 12 months pre- and post-CTA. Results: Patients were 50 ± 12 years of

age (59% men), with 34%, 47%, and 33% on baseline statin, BP medication(s), and aspirin,

respectively. Relative to patients without CAD (n = 617), patients with nonobstructive (n = 411)

and obstructive CAD (n = 97) demonstrated significant intensification in unadjusted rates of

statin (26%, 46%, and 46% of patients; p < 0.001), BP (11%, 21%, and 24%; p < 0.001), and

aspirin therapies (9%, 29%, and 40%; p < 0.001), and significant improvements in total

cholesterol (-6.7, -14.7, and -24.7 mg/dl; p = 0.008), low-density lipoprotein cholesterol (-5.6, -

14.1, and -24.6 mg/dl; p = 0.001), systolic (+0.1, -1.4, and -4.9 mm Hg; p = 0.002), and diastolic

BP (-0.6, -1.0, and -3.4 mm Hg;  $p = 0.012$ ), respectively. Adjusted for baseline risk factors and medications, CAD was independently associated with increased aspirin, statin, and BP medication use rates in CTA-identified nonobstructive CAD (odds ratio [OR]: 6.9, 95% confidence interval [CI]: 4.7 to 10.2; OR: 6.6, 95% CI: 3.0 to 14.3; OR: 1.6, 95% CI: 1.1 to 2.2, respectively;  $p < 0.05$ ), and aspirin and statin use in obstructive CAD (OR: 42.4, 95% CI: 15.8 to 113.9; OR: 30.3, 95% CI: 3.2 to 289.2, respectively;  $p < 0.05$ ). Conclusions: CAD presence and severity on CTA are associated with increased use of preventive cardiovascular medications and improvements in cholesterol and BP. ?? 2013 American College of Cardiology Foundation.",

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"parse-names" : false, "suffix" : "" } ], "container-title" : "JACC: Cardiovascular Imaging", "id" :  
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"27081014", "abstract" : "Background In a prospective, multicenter, randomized controlled trial,  
4,146 patients were randomized to receive standard care or standard care plus coronary  
computed tomography angiography (CCTA). Objectives The purpose of this study was to  
explore the consequences of CCTA-assisted diagnosis on invasive coronary angiography,  
preventive treatments, and clinical outcomes. Methods In post hoc analyses, we assessed  
changes in invasive coronary angiography, preventive treatments, and clinical outcomes using  
national electronic health records. Results Despite similar overall rates (409 vs. 401;  $p = 0.451$ ),  
invasive angiography was less likely to demonstrate normal coronary arteries (20 vs. 56; hazard  
ratios [HRs]: 0.39 [95% confidence interval (CI): 0.23 to 0.68];  $p < 0.001$ ) but more likely to  
show obstructive coronary artery disease (283 vs. 230; HR: 1.29 [95% CI: 1.08 to 1.55];  $p =$   
0.005) in those allocated to CCTA. More preventive therapies (283 vs. 74; HR: 4.03 [95% CI: 3.12  
to 5.20];  $p < 0.001$ ) were initiated after CCTA, with each drug commencing at a median of 48  
to 52 days after clinic attendance. From the median time for preventive therapy initiation (50

days), fatal and nonfatal myocardial infarction was halved in patients allocated to CCTA compared with those assigned to standard care (17 vs. 34; HR: 0.50 [95% CI: 0.28 to 0.88];  $p = 0.020$ ). Cumulative 6-month costs were slightly higher with CCTA: difference \$462 (95% CI: \$303 to \$621). Conclusions In patients with suspected angina due to coronary heart disease, CCTA leads to more appropriate use of invasive angiography and alterations in preventive therapies that were associated with a halving of fatal and non-fatal myocardial infarction.

(Scottish COmputed Tomography of the HEART Trial [SCOT-HEART]; NCT01149590).", "author" :

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"0735-1097", "ISSN" : "07351097", "PMID" : "28385304", "abstract" : "BACKGROUND The choice  
of either anatomical or functional noninvasive testing to evaluate suspected coronary artery  
disease might affect subsequent clinical management and outcomes. OBJECTIVES This study

analyzed the association of initial noninvasive cardiac testing in outpatients with stable symptoms, with subsequent use of medications, invasive procedures, and clinical outcomes.

**METHODS** We studied patients enrolled in a Danish nationwide register who underwent initial noninvasive cardiac testing with either coronary computed tomography angiography (CTA) or functional testing (exercise electrocardiography or nuclear stress testing) from 2009 to 2015.

Further use of noninvasive testing, invasive procedures, medications, and medical costs within 120 days were evaluated. Risks of long-term mortality and myocardial infarction (MI) were

analyzed using adjusted Cox proportional hazard models. **RESULTS** A total of 86,705 patients

underwent either functional testing (n= 53,744, mean age 57.4 years, 49% males) or

coronary CTA (n= 32,961, mean age 57.4 years, 45% males), and were followed for a

median of 3.6 years. Compared with functional testing, there was significantly higher use

of statins (15.9% vs. 9.1%), aspirin (12.7% vs. 8.5%), invasive coronary angiography (14.7% vs.

10.1%), and percutaneous coronary intervention (3.8% vs. 2.1%); all  $p < 0.001$  after

coronary CTA. The mean costs of subsequent testing, invasive procedures, and medications

were higher after coronary CTA (\$995 vs. \$718;  $p < 0.001$ ). Unadjusted rates of mortality

(2.1% vs. 4.0%) and MI hospitalization (0.8% vs. 1.5%) were lower after coronary CTA than

functional testing (both  $p < 0.001$ ). After adjustment, coronary CTA was associated with

a comparable all-cause mortality (hazard ratio: 0.96; 95% confidence interval: 0.88 to 1.05), and

a lower risk of MI (hazard ratio: 0.71; 95% confidence interval: 0.61 to 0.82). **CONCLUSIONS** In



stable patients undergoing initial evaluation for suspected coronary artery disease, coronary CTA was associated with greater use of statins, aspirin, and invasive procedures, and higher costs than functional testing. Wu00a0Coronary CTA was associated with a lower risk of MI, but a similar risk of all-cause mortality.", "author" : [ { "dropping-particle" : "", "family" :

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Tomography Angiography in Patients With Stable Coronary Artery Disease", "type" :

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"<sup><sup>43</sup>Wu2013<sup>45</sup></sup>" }, "properties" : { }, "schema" :

"https://github.com/citation-style-language/schema/raw/master/csl-citation.json" } } Given the

additive prognostic benefit of multi-site screening WB-MRA may prove to be an even more powerful tool for disease detection and risk stratification.

It could be argued that since patients with clinically apparent cardiovascular disease in one site

will result in patients being treated for atherosclerotic risk factors that further information

about disease elsewhere is superfluous. However this ignores several factors. Two trials have

demonstrated benefit for carotid endarterectomy in asymptomatic individuals with incidentally

detected carotid stenosis >70%.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1",

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(Electronic)W0140-6736 (Linking)", "ISSN" : "01406736", "PMID" : "15135594", "abstract" :

"Background Among patients with substantial carotid artery narrowing but no recent

neurological symptom (stroke or transient ischaemia), the balance of surgical risks and long-

term benefits from carotid endarterectomy (CEA) was unclear. Methods During 1993-2003, 3120 asymptomatic patients with substantial carotid narrowing were randomised equally between immediate CEA (half got CEA by 1 month, 88% by 1 year) and indefinite deferral of any CEA (only 4% per year got CEA) and were followed for up to 5 years (mean 3.4 years). Kaplan-Meier analyses of 5-year risks are by allocated treatment. Findings The risk of stroke or death within 30 days of CEA was 3.1% (95% CI 2.3-4.1). Comparing all patients allocated immediate CEA versus all allocated deferral, but excluding such perioperative events, the 5-year stroke risks were 3.8% versus 11% (gain 7.2% [95% CI 5.0-9.4],  $p < 0.0001$ ). This gain chiefly involved carotid territory ischaemic strokes (2.7% vs 9.5%; gain 6.8% [4.8-8.8],  $p < 0.0001$ ), of which half were disabling or fatal (1.6% vs 5.3%; gain 3.7% [2.1-5.2],  $p < 0.0001$ ), as were half the perioperative strokes. Combining the perioperative events and the non-perioperative strokes, net 5-year risks were 6.4% versus 11.8% for all strokes (net gain 5.4% [3.0-7.8],  $p < 0.0001$ ), 3.5% versus 6.1% for fatal or disabling strokes (net gain 2.5% [0.8-4.3],  $p = 0.004$ ), and 2.1% versus 4.2% just for fatal strokes (net gain 2.1% [0.6-3.6],  $p = 0.006$ ). Subgroup-specific analyses found no significant heterogeneity in the perioperative hazards or (apart from the importance of cholesterol) in the long-term postoperative benefits. These benefits were separately significant for males and females; for those with about 70%, 80%, and 90% carotid artery narrowing on ultrasound; and for those younger than 65 and 65-74 years of age (though not for older patients, half of whom die

within 5 years from unrelated causes). Full compliance with allocation to immediate CEA or deferral would, in expectation, have produced slightly bigger differences in the numbers operated on, and hence in the net 5-year benefits. The 10-year benefits are not yet known.

**Interpretation** In asymptomatic patients younger than 75 years of age with carotid diameter reduction about 70% or more on ultrasound (many of whom were on aspirin, antihypertensive, and, in recent years, statin therapy), immediate CEA halved the net 5-year stroke risk from

about 12% to about 6% (including the 3% perWu2026", "author" : [ { "dropping-particle" : "", "family" : "Asymptomatic", "given" : "M R C", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Surgery", "given" : "Carotid", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Acst", "given" : "Trial", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Group", "given" : "Collaborative", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Lancet", "id" : "ITEM-1", "issue" : "9420", "issued" : { "date-parts" : [ [ "2004" ] ] }, "page" : "1491-1502", "title" : "Prevention of disabling and fatal strokes by successful carotid endarterectomy in patients without recent neurological symptoms: Randomised controlled trial", "type" : "article-journal", "volume" : "363" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=3815cb2b-efa4-4fcb-864a-0fcd6c2eb9f2" ] ], { "id" : "ITEM-2", "itemData" : { "ISSN" : "0098-7484", "PMID" : "7723155", "abstract" : "OBJECTIVE

To determine whether the addition of carotid endarterectomy to aggressive medical

management can reduce the incidence of cerebral infarction in patients with asymptomatic carotid artery stenosis. DESIGN Prospective, randomized, multicenter trial. SETTING Thirty-nine clinical sites across the United States and Canada. PATIENTS Between December 1987 and December 1993, a total of 1662 patients with asymptomatic carotid artery stenosis of 60% or greater reduction in diameter were randomized; follow-up data are available on 1659. At baseline, recognized risk factors for stroke were similar between the two treatment groups. INTERVENTION Daily aspirin administration and medical risk factor management for all patients; carotid endarterectomy for patients randomized to receive surgery. MAIN OUTCOME MEASURES Initially, transient ischemic attack or cerebral infarction occurring in the distribution of the study artery and any transient ischemic attack, stroke, or death occurring in the perioperative period. In March 1993, the primary outcome measures were changed to cerebral infarction occurring in the distribution of the study artery or any stroke or death occurring in the perioperative period. RESULTS After a median follow-up of 2.7 years, with 4657 patient-years of observation, the aggregate risk over 5 years for ipsilateral stroke and any perioperative stroke or death was estimated to be 5.1% for surgical patients and 11.0% for patients treated medically (aggregate risk reduction of 53% [95% confidence interval, 22% to 72%]). CONCLUSION Patients with asymptomatic carotid artery stenosis of 60% or greater reduction in diameter and whose general health makes them good candidates for elective surgery will have a reduced 5-year risk of ipsilateral stroke if carotid endarterectomy performed with less

than 3% perioperative morbidity and mortality is added to aggressive management of

modifiable risk factors.", "container-title" : "JAMA", "id" : "ITEM-2", "issue" : "18", "issued" : {

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asymptomatic carotid artery stenosis. Executive Committee for the Asymptomatic Carotid

Atherosclerosis Study.", "type" : "article-journal", "volume" : "273" }, "uris" : [

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these the CREST-2 trial is awaited to determine the role of carotid artery stenting in this arena,

and whether the benefits of carotid endarterectomy seen in these two previous trials hold true

in the context of more modern optimal medical therapy strategies.{ADDIN CSL\_CITATION {

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Recognition of unrecognised myocardial infarctions through the incorporation of a cardiac MRI into the WBMRA protocol can also yield significant changes in management. These silent myocardial infarcts have the same prognostic implications as recognised myocardial infarcts and are present in approximately 20% of seventy year olds and 30% of those with PAD.

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Health Study (CHS) database, composed of individuals  $\geq 65$ , was queried for participants who, at entry, demonstrated electrocardiographic evidence of a prior Q-wave MI, but who lacked a history of this diagnosis. The features and outcomes of this group were compared to those of individuals with prevalent RMI. RESULTS: Of 5,888 participants, 901 evidenced a past MI, and 201 (22.3%) were previously unrecognized. The independent predictors of UMI were the absence of angina and the absence of congestive heart failure (CHF). Six-year mortality did not significantly differ between the two groups. CONCLUSIONS: 1) In the elderly, UMI continues to represent a significant proportion of all MIs; 2) associations with angina and CHF may reflect complex neurological issues, but they also may represent diagnosis bias; 3) these individuals can otherwise not be distinguished from those with recognized infarctions; and 4) mortality rates after UMI and RMI are similar. Future studies should address screening for UMI, risk stratification after detection of previously UMI, and the role of standard post-MI therapies.", "author" : [ { "dropping-particle" : "", "family" : "Sheifer", "given" : "S E", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Gersh", "given" : "B J", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Yanez", "given" : "N D", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Ades", "given" : "P A", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Burke", "given" : "G L", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, {



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myocardial infarction in the elderly.", "type" : "article-journal", "volume" : "35" }, "uris" : [  
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"PMID" : "27430315", "abstract" : "BACKGROUND Individuals with unrecognized myocardial  
infarctions (UMIs) detected with cardiovascular magnetic resonance (CMR) constitute a recently  
defined group whose prognosis has not been fully evaluated. However, increasing evidence  
indicate that these individuals may be at considerable cardiovascular risk. The aim of the  
present study was to investigate the prognostic impact of CMR detected UMIs for major  
adverse cardiac events (MACE) in community living elderly individuals. METHODS Late  
gadolinium enhancement CMR was performed in 248 randomly chosen 70-year-olds.  
Individuals with myocardial infarction (MI) scars, with or without a hospital diagnosis of MI  
were classified as recognized MI (RMI) or UMI, respectively. Medical records and death  
certificates were scrutinized. MACE was defined as cardiac death, non-fatal MI, a new diagnosis  
of angina pectoris, or symptom-driven coronary artery revascularization. RESULTS During  
follow-up (mean 11 years) MACE occurred in 10% (n=18/182) of

the individuals without MI scars, in 20% (n=11/55) of the individuals with UMI, and in 45% (n=5/11) of the individuals with RMI, with a significant difference between the UMI group and the group without MI scars (p=0.045), and between the RMI group and the group without MI scars (p=0.0004). Cardiac death and/or non-fatal MI occurred in 15, 5, and 3 of the individuals in the NoMI, UMI, and RMI group respectively. Hazards ratios for MACE adjusted for risk factors and sex were 2.55 (95% CI 1.20-5.42; p=0.015) for UMI and 3.28 (95% CI 1.16-9.22; p=0.025) for RMI. CONCLUSIONS The presence of a CMR detected UMI entailed a more than double risk for MACE in community living 70-year-old individuals.

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for Cardiovascular Magnetic Resonance", "id" : "ITEM-2", "issue" : "1", "issued" : { "date-parts" : [ [ "2016" ] ] }, "page" : "43", "publisher" : "Journal of Cardiovascular Magnetic Resonance", "title" : "Long-term prognosis of unrecognized myocardial infarction detected with cardiovascular magnetic resonance in an elderly population.", "type" : "article-journal", "volume" : "18" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=d76ca4a1-01bc-486a-ab56-7672d9f1b30d" ] }, { "id" : "ITEM-3", "itemData" : { "DOI" : "10.1186/s12880-016-0121-4", "ISSN" : "14712342", "abstract" : "Wu00a9 2016 Weir-McCall et al. Background: The aim of this study was to use whole body cardiovascular magnetic resonance imaging (WB CVMR) to assess the heart and arterial network in a single examination, so as to describe the burden of atherosclerosis and subclinical disease in participants with symptomatic single site vascular disease. Methods: 64 patients with a history of symptomatic single site vascular disease (38 coronary artery disease (CAD), 9 cerebrovascular disease, 17 peripheral arterial disease (PAD)) underwent whole body angiogram and cardiac MR in a 3 T scanner. The arterial tree was subdivided into 31 segments and each scored according to the degree of stenosis. From this a standardised atheroma score (SAS) was calculated. Cine and late gadolinium enhancement images of the left ventricle were obtained. Results: Asymptomatic atherosclerotic disease with greater than 50 % stenosis in arteries other than that responsible for their presenting complain was detected in 37 % of CAD, 33 % of cerebrovascular and 47 % of PAD patients. Unrecognised myocardial infarcts were observed in 29 % of PAD patients. SAS was significantly higher in PAD patients 24 (17.5-

30.5) compared to CAD 4 (2-11.25) or cerebrovascular disease patients 6 (2-10) (ANCOVA  $p < 0.001$ ). Standardised atheroma score positively correlated with age ( $r = 0.36$   $p = 0.002$ ), smoking status ( $r = 0.34$   $p = 0.002$ ), and LV mass ( $r = -0.61$   $p = 0.001$ ) on multiple linear regression. Conclusion: WB CVMR is an effective method for the stratification of cardiovascular disease. The high prevalence of asymptomatic arterial disease, and silent myocardial infarctions, particularly in the peripheral arterial disease group, demonstrates the importance of a systematic approach to the assessment of cardiovascular disease.", "author" : [ { "dropping-particle" : "", "family" : "Weir-McCall", "given" : "J.R.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Duce", "given" : "S.L.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Gandy", "given" : "S.J.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Matthew", "given" : "S.Z.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Martin", "given" : "P.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Cassidy", "given" : "D.B.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "McCormick", "given" : "L.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Belch", "given" : "J.J.F.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Struthers", "given" : "A.D.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }

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"Whole body cardiovascular magnetic resonance imaging to stratify symptomatic and
asymptomatic atherosclerotic burden in patients with isolated cardiovascular disease", "type" :
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"<sup><sup>49</sup>Wu2013<sup>51</sup></sup>" }, "properties" : { }, "schema" :
"https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }} Furthermore
these patients respond well to both conventional secondary prevention medication and
percutaneous coronary intervention.{ADDIN CSL_CITATION { "citationItems" : [ { "id" : "ITEM-1",
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7484 (Linking)", "ISSN" : "1538-3598", "PMID" : "17488963", "abstract" : "CONTEXT: The effect of
a percutaneous coronary intervention (PCI) on the long-term prognosis of patients with silent
ischemia after a myocardial infarction (MI) is not known. OBJECTIVE: To determine whether PCI
compared with drug therapy improves long-term outcome of asymptomatic patients with silent

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ischemia after an MI. DESIGN, SETTING, AND PARTICIPANTS: Randomized, unblinded, controlled trial (Swiss Interventional Study on Silent Ischemia Type II [SWISSI II]) conducted from May 2, 1991, to February 25, 1997, at 3 public hospitals in Switzerland of 201 patients with a recent MI, silent myocardial ischemia verified by stress imaging, and 1- or 2-vessel coronary artery disease. Follow-up ended on May 23, 2006. INTERVENTIONS: Percutaneous coronary intervention aimed at full revascularization (n = 96) or intensive anti-ischemic drug therapy (n = 105). All patients received 100 mg/d of aspirin and a statin. MAIN OUTCOME MEASURES: Survival free of major adverse cardiac events defined as cardiac death, nonfatal MI, and/or symptom-driven revascularization. Secondary measures included exercise-induced ischemia and resting left ventricular ejection fraction during follow-up. RESULTS: During a mean (SD) follow-up of 10.2 (2.6) years, 27 major adverse cardiac events occurred in the PCI group and 67 events occurred in the anti-ischemic drug therapy group (adjusted hazard ratio, 0.33; 95% confidence interval, 0.20-0.55;  $P < .001$ ), which corresponds to an absolute event reduction of 6.3% per year (95% confidence interval, 3.7%-8.9%;  $P < .001$ ). Patients in the PCI group had lower rates of ischemia (11.6% vs 28.9% in patients in the drug therapy group at final follow-up;  $P = .03$ ) despite fewer drugs. Left ventricular ejection fraction remained preserved in PCI patients (mean [SD] of 53.9% [9.9%] at baseline to 55.6% [8.1%] at final follow-up) and decreased significantly ( $P < .001$ ) in drug therapy patients (mean [SD] of 59.7% [11.8%] at baseline to 48.8% [7.9%] at final follow-up). CONCLUSION: Among patients with

recent MI, silent myocardial ischemia verified by stress imaging, and 1- or 2-vessel coronary artery disease, PCI compared with anti-ischemic drug therapy reduced the long-term risk of major cardiac events. TRIAL REGISTRATION: clinicaltrials.gov Identifier: NCT00387231.", "author" : [ { "dropping-particle" : "", "family" : "Erne", "given" : "Paul", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Schoenenberger", "given" : "Andreas W", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Burckhardt", "given" : "Dieter", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Zuber", "given" : "Michel", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Kiowski", "given" : "Wolfgang", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Buser", "given" : "Peter T", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Dubach", "given" : "Paul", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Resink", "given" : "Therese J", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Pfisterer", "given" : "Matthias", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "JAMA : the journal of the American Medical Association", "id" : "ITEM-1", "issue" : "18", "issued" : { "date-parts" : [ [ "2007", "5", "9" ] ] }, "page" : "1985-91", "title" : "Effects of percutaneous coronary interventions in silent ischemia after myocardial infarction: the SWISSI II randomized controlled

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: "17644512", "abstract" : "AIMS: To determine the effect of anti-ischaemic drug therapy on

long-term outcomes of asymptomatic patients without coronary artery disease (CAD) history

but silent exercise ST-depression. METHODS AND RESULTS: In a randomized multicentre trial,

263 of 522 asymptomatic subjects without CAD but at least one CAD risk factor in whom silent

ischaemia by exercise ECG was confirmed by stress imaging were asked to participate. The 54

(21%) consenting patients were randomized to anti-anginal drug therapy in addition to risk

factor control (MED, n = 26) or risk factor control-only (RFC, n = 28). They were followed yearly

for 11.2 +/- 2.2 years. During 483 patient-years, cardiac death, non-fatal myocardial infarction,

or acute coronary syndrome requiring hospitalization or revascularization occurred in 3 (12%)

of MED vs. 17 (61%) of RFC patients (P < 0.001). In addition, MED patients had consistently

lower rates of exercise-induced ischaemia during follow-up, and left ventricular ejection

fraction remained unchanged (-0.7%, P = 0.597) in contrast to RFC patients in whom it

decreased over time (-6.0%, P = 0.006). CONCLUSION: Anti-ischaemic drug therapy and aspirin

seem to reduce cardiac events in subjects with asymptomatic ischaemia type I. In such patients,

exercise-induced ST-segment depression should be verified by stress imaging; if silent

ischaemia is documented, anti-ischaemic drug therapy and aspirin should be considered.",



"author" : [ { "dropping-particle" : "", "family" : "Erne", "given" : "Paul", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Schoenenberger", "given" : "Andreas W", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Zuber", "given" : "Michel", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Burckhardt", "given" : "Dieter", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Kiowski", "given" : "Wolfgang", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Dubach", "given" : "Paul", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Resink", "given" : "Therese", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Pfisterer", "given" : "Matthias", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "European heart journal", "id" : "ITEM-2", "issue" : "17", "issued" : { "date-parts" : [ [ "2007", "9" ] ] }, "page" : "2110-7", "title" : "Effects of anti-ischaemic drug therapy in silent myocardial ischaemia type I: the Swiss Interventional Study on Silent Ischaemia type I (SWISSI I): a randomized, controlled pilot study.", "type" : "article-journal", "volume" : "28" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=59649100-8176-4b9b-933e-a50101269f83" ] }, { "id" : "ITEM-3", "itemData" : { "DOI" : "10.1016/j.ahj.2004.07.027", "ISSN" : "1097-6744", "PMID" : "15846252", "abstract" : "BACKGROUND: Evaluated the efficacy of reducing the risk of cardiac

events by a preclinical diagnosis of CAD in subjects with type 2 diabetes mellitus with 2 or more cardiovascular risk factors. METHODS: One hundred forty-one subjects with type 2 diabetes mellitus without known cardiac disease and asymptomatic, aged >45 to <76 years, were randomized into the screening arm for CAD (71 patients) or to the control arm (70 patients). The screening consisted in performing an exercise electrocardiogram test and dipyridamole stress echocardiography; if 1 test was abnormal, coronary angiography is done. Screening was positive in 15 subjects (21.4%). At coronary angiography, which was performed in 14 of 15 patients, stenoses  $\geq 50\%$  of vessel diameter were present in 9 patients, of these 4 underwent coronary artery bypass grafting and 4 underwent percutaneous transluminal coronary angioplasty. Stenoses  $< 50\%$  of vessel diameter were present in 5 patients. RESULTS: Mean follow-up was 53.5 months (range, 42-54 months). During this period, 1 major (myocardial infarction) and 3 minor events (angina) occurred in the screening arm. Eleven major and 4 minor events occurred in the control arm. In the screened arm, the proportion of all events was significantly less ( $P = .018$ ) (RR .226, 95% CI 0.0707-0.719,  $P = .012$ ); the proportion of major to minor events was significantly less ( $P = .006$ ) (RR .07, 95% CI 0.0087-0.565,  $P = .013$ ). CONCLUSIONS: The preclinical diagnosis of CAD is effective in reducing the risk of cardiac events, especially major events, in subjects with type 2 diabetes mellitus at high cardiovascular risk.", "author" : [ { "dropping-particle" : "", "family" : "Faglia", "given" : "Ezio", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "",

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"Risk reduction of cardiac events by screening of unknown asymptomatic coronary artery

disease in subjects with type 2 diabetes mellitus at high cardiovascular risk: an open-label

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important as secondary prevention strategies differ between anatomical territories, in particular with beta-blockers recommended in those with myocardial infarcts due to their benefit in mortality reduction, but are not indicated in those with cerebrovascular or peripheral arterial disease.

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1Societie: European Society of Cardiology (ESC)2Societie: European

Association for the Study of Diabetes (EASD)3Societie: European Atherosclerosis Society

(EAS)4Societie: European Heart Network (EHN)5Societie: European Society of Hypertension

(ESH)6Societie: European Stroke Organisation (ESO)7International Diabetes Federation

European Region (IDF Europe)8International Federation of Sport Medicine (FIMS)9International

Society of Behavioural Medicine (ISBM)10WONCA Europe. The disclosure forms of all experts

involved in the development of these guidelines are available on the ESC website

<http://www.escardio.org/guidelines>. ESC Committee for Practice Guidelines (CPG) and National

Cardiac Societies document reviewers: listed in the Appendix. ESC entities having participated in

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WB-MRA also provides additional prognostic information. Multisite disease is associated with  
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manifestation of systemic atherosclerosis that is common and is associated with an increased risk of death and ischemic events, yet may be underdiagnosed in primary care practice.

OBJECTIVE: To assess the feasibility of detecting PAD in primary care clinics, patient and physician awareness of PAD, and intensity of risk factor treatment and use of antiplatelet therapies in primary care clinics. DESIGN AND SETTING: The PAD Awareness, Risk, and Treatment: New Resources for Survival (PARTNERS) program, a multicenter, cross-sectional study conducted at 27 sites in 25 cities and 350 primary care practices throughout the United States in June-October 1999. PATIENTS: A total of 6979 patients aged 70 years or older or aged 50 through 69 years with history of cigarette smoking or diabetes were evaluated by history and by measurement of the ankle-brachial index (ABI). PAD was considered present if the ABI was 0.90 or less, if it was documented in the medical record, or if there was a history of limb revascularization. Cardiovascular disease (CVD) was defined as a history of atherosclerotic coronary, cerebral, or abdominal aortic aneurysmal disease. MAIN OUTCOME MEASURES: Frequency of detection of PAD; physician and patient awareness of PAD diagnosis; treatment intensity in PAD patients compared with treatment of other forms of CVD and with patients without clinical evidence of atherosclerosis. RESULTS: PAD was detected in 1865 patients (29%); 825 of these (44%) had PAD only, without evidence of CVD. Overall, 13% had PAD only, 16% had PAD and CVD, 24% had CVD only, and 47% had neither PAD nor CVD (the reference group). There were 457 patients (55%) with newly diagnosed PAD only and 366

(35%) with PAD and CVD who were newly diagnosed during the survey. Eighty-three percent of patients with prior PAD were aware of their diagnosis, but only 49% of physicians were aware of this diagnosis. Among patients with PAD, classic claudication was distinctly uncommon (11%). Patients with PAD had similar atherosclerosis risk factor profiles compared with those who had CVD. Smoking behavior was more frequently treated in patients with new (53%) and prior PAD (51%) only than in those with CVD only (35%;  $P < .001$ ). Hypertension was treated less frequently in new (84%) and prior PAD (88%) only vs CVD only (95%;  $P < .001$ ) and hyperlipidemia was treated less frequently in new (44%) and prior PAD (56%) only vs CVD only (73%,  $P < .001$ ).

Antiplatelet therapy was more frequently used in patients with new (53%) and prior PAD (51%) only than in those with CVD only (35%;  $P < .001$ ).

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with identifying which patients are highest risk for cardiovascular events. Prior ischemic events,  
polyvascular disease, and diabetes mellitus have all been identified as predictors of ischemic  
events, but their comparative contributions to future risk remain unclear. OBJECTIVE: To  
categorize the risk of cardiovascular events in stable outpatients with various initial  
manifestations of atherothrombosis using simple clinical descriptors. DESIGN, SETTING, AND  
PATIENTS: Outpatients with coronary artery disease, cerebrovascular disease, or peripheral  
arterial disease or with multiple risk factors for atherothrombosis were enrolled in the global

Reduction of Atherothrombosis for Continued Health (REACH) Registry and were followed up for as long as 4 years. Patients from 3647 centers in 29 countries were enrolled between 2003 and 2004 and followed up until 2008. Final database lock was in April 2009. MAIN OUTCOME MEASURES: Rates of cardiovascular death, myocardial infarction, and stroke. RESULTS: A total of 45,227 patients with baseline data were included in this 4-year analysis. During the follow-up period, a total of 5481 patients experienced at least 1 event, including 2315 with cardiovascular death, 1228 with myocardial infarction, 1898 with stroke, and 40 with both a myocardial infarction and stroke on the same day. Among patients with atherothrombosis, those with a prior history of ischemic events at baseline (n = 21,890) had the highest rate of subsequent ischemic events (18.3%; 95% confidence interval [CI], 17.4%-19.1%); patients with stable coronary, cerebrovascular, or peripheral artery disease (n = 15,264) had a lower risk (12.2%; 95% CI, 11.4%-12.9%); and patients without established atherothrombosis but with risk factors only (n = 8073) had the lowest risk (9.1%; 95% CI, 8.3%-9.9%) (P < .001 for all comparisons). In addition, in multivariable modeling, the presence of diabetes (hazard ratio [HR], 1.44; 95% CI, 1.36-1.53; P < .001), an ischemic event in the previous year (HR, 1.71; 95% CI, 1.57-1.85; P < .001), and polyvascular disease (HR, 1.99; 95% CI, 1.78-2.24; P < .001) each were associated with a significantly higher risk of the primary end point. CONCLUSION: Clinical descriptors can assist clinicians in identifying high-risk patients within the broad range of risk for outpatients with atherothrombosis.", "author" : [ { "dropping-particle" : "", "family" : "Bhatt",

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setting. Differential event rates for patients with documented coronary artery disease (CAD), cerebrovascular disease (CVD), or peripheral arterial disease (PAD) or those at risk of these diseases have not been previously evaluated in a single international cohort. OBJECTIVE: To establish contemporary, international, 1-year CV event rates in outpatients with established arterial disease or with multiple risk factors for atherothrombosis. DESIGN, SETTING, AND PARTICIPANTS: The Reduction of Atherothrombosis for Continued Health (REACH) Registry is an international, prospective cohort of 68 236 patients with either established atherosclerotic arterial disease (CAD, PAD, CVD; n = 55 814) or at least 3 risk factors for atherothrombosis (n = 12 422), who were enrolled from 5587 physician practices in 44 countries in 2003-2004. MAIN OUTCOME MEASURES: Rates of CV death, myocardial infarction (MI), and stroke. RESULTS: As of July 2006, 1-year outcomes were available for 95.22% (n = 64 977) of participants. Cardiovascular death, MI, or stroke rates were 4.24% overall: 4.69% for those with established atherosclerotic arterial disease vs 2.15% for patients with multiple risk factors only. Among patients with established disease, CV death, MI, or stroke rates were 4.52% for patients with CAD, 6.47% for patients with CVD, and 5.35% for patients with PAD. The incidences of the end point of CV death, MI, or stroke or of hospitalization for atherothrombotic event(s) were 15.20% for CAD, 14.53% for CVD, and 21.14% for PAD patients with established disease. These event rates increased with the number of symptomatic arterial disease locations, ranging from 5.31% for patients with risk factors only to 12.58% for patients with 1, 21.14% for patients with

2, and 26.27% for patients with 3 symptomatic arterial disease locations ( $P < .001$  for trend).

CONCLUSIONS: In this large, contemporary, international study, outpatients with established atherosclerotic arterial disease, or at risk of atherothrombosis, experienced relatively high annual CV event rates. Multiple disease locations increased the 1-year risk of CV events.",

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current therapeutic strategies of statins and antihypertensives are cheap, newer monoclonal
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affecting lipid levels may reduce the risk of cardiovascular disease. Yet, the inflammatory
hypothesis of atherothrombosis has remained unproved. MethodsWe conducted a randomized,
double-blind trial of canakinumab, a therapeutic monoclonal antibody targeting interleukin-

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1Wu03b2, involving 10,061 patients with previous myocardial infarction and a high-sensitivity C-reactive protein level of 2 mg or more per liter. The trial compared three doses of canakinumab (50 mg, 150 mg, and 300 mg, administered subcutaneously every 3 months) with placebo. The primary efficacy end point was nonfatal myocardial infarction, nonfatal stroke, or cardiovascular death. ResultsAt 48 months, the median reduction from baseline in the high-sensitivity C-reactive protein level was 26 percentage points greater in the group that received the 50-mg dose of canakinumab, 37 percentage points greater in the 150-mg group, and 41 percentage points greater in t...

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 cholesterol levels by approximately 60%. Whether it prevents cardiovascular events is uncertain.  
 MethodsWe conducted a randomized, double-blind, placebo-controlled trial involving 27,564  
 patients with atherosclerotic cardiovascular disease and LDL cholesterol levels of 70 mg per

deciliter (1.8 mmol per liter) or higher who were receiving statin therapy. Patients were randomly assigned to receive evolocumab (either 140 mg every 2 weeks or 420 mg monthly) or matching placebo as subcutaneous injections. The primary efficacy end point was the composite of cardiovascular death, myocardial infarction, stroke, hospitalization for unstable angina, or coronary revascularization. The key secondary efficacy end point was the composite of cardiovascular death, myocardial infarction, or stroke. The median duration of follow-up was 2.2 years. Results

At 48 weeks, the ...", "author" : [ { "dropping-particle" : "", "family" : "Sabatine", "given" : "Marc S.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Giugliano", "given" : "Robert P.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Keech", "given" : "Anthony C.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Honarpour", "given" : "Narimon", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Wiviott", "given" : "Stephen D.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Murphy", "given" : "Sabina A.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Kuder", "given" : "Julia F.", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Wang", "given" : "Huei", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Liu", "given" : "Thomas", "non-dropping-particle" : "", "parse-names" :

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In a clinical setting the most immediate application of WB-MRA is to extend already clinically indicated MRA exams. The cost effectiveness of extending clinically indicated single site MRA into a WB-MRA plus cardiac MRI has been previously demonstrated in those with peripheral artery disease. The extension of the study added only a small cost to the overall cost of the planned MRA and reduced overall healthcare costs due to reduced downstream resource

utilization.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1016/j.hlpt.2013.08.003", "ISSN" : "22118837", "author" : [ { "dropping-particle" : "", "family" : "Gassull", "given" : "Daniel", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Schulthess", "given" : "Duane", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Suttie", "given" : "Stuart", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Houston", "given" : "Graeme", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Health Policy and Technology", "id" : "ITEM-1", "issue" : "4", "issued" : { "date-parts" : [ [ "2013", "12" ] ] }, "page" : "181-187", "publisher" : "Elsevier", "title" : "Whole-Body Magnetic Resonance Angiography (WBMRA) as a tool for driving efficiency in the cost and treatment of Claudication Co-morbidities", "type" : "article-journal", "volume" : "2" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=272cdeb2-0d02-4c8f-aa0c-7cf630f2b0ed" ] } ], "mendeley" : { "formattedCitation" : "<sup><sup>60</sup></sup>", "plainTextFormattedCitation" : "60", "previouslyFormattedCitation" : "<sup><sup>60</sup></sup>", "properties" : { }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" } } Further studies are now needed to determine if the cost savings seen in a PAD population are extendable to those with coronary or cerebrovascular disease where total atheroma burden is known to be less than that of PAD.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" :

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imaging to stratify symptomatic and asymptomatic atherosclerotic burden in patients with isolated cardiovascular disease", "type" : "article-journal", "volume" : "16" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=f1b7e761-b441-4bbc-81d9-d469ca27688a" ] } ], "mendeley" : { "formattedCitation" : "<sup><sup>40</sup></sup>", "plainTextFormattedCitation" : "40", "previouslyFormattedCitation" : "<sup><sup>40</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-style-language/schema/raw/master/csl-citation.json" }}

## Vasculitis

Atherosclerosis is not the only systemic vascular disease. Large vessel vasculitides such as giant cell arteritis (GCA) and Takayasu's Arteritis (TA) have a systemic distribution. Type V TA arises when the neck, thoracic, abdominal and pelvic vessels are involved and occurs in 55% of cases.

{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1016/j.ijcard.2011.01.094", "ISBN" : "1874-1754 (Electronic) 0167-5273 (Linking)", "ISSN" : "01675273", "PMID" : "21354639", "abstract" : "Takayasu's arteritis (TA) is primary vasculitis.

Cardiac involvements in TA is due to the consequences of the vascular lesions as well as the primary pathology of the heart. The disease activity of TA is known to influence the prognosis of TA. We hypothesized that the cardiovascular involvement of TA is related to the disease activity. We evaluated the cardiovascular manifestations of TA, and we assessed their relation

to the disease activity of TA. Two hundred four patients were diagnosed with TA from September, 1994 to March, 2009 according to the diagnostic criteria of the 1990 American College of Rheumatology. Their clinical features and the laboratory, angiographic and echocardiographic findings were retrospectively reviewed. The group with active disease activity was defined as satisfying one of the following criteria: i) an elevated ESR or CRP level, ii) thickened arterial wall with mural enhancement on CT or MR angiography, and iii) carotidynia at the time of the initial diagnosis. One hundred thirty nine patients (69.2%) were classified as the active group. The cardiovascular signs and symptoms were not generally different between the active and inactive groups. The active TA patients had more frequent involvement of the ascending aorta and the aortic arch and its main branches than did the inactive group. The active group showed a higher incidence of significant aortic valve regurgitation and pulmonary hypertension, and a higher level of NT-proBNP. These findings suggest that disease activity plays an important role for the cardiovascular manifestations of TA. The TA patients with higher activity have more cardiovascular morbidity compared to the TA patients with low disease activity. Wu00a9 2011 Elsevier Ireland Ltd. All rights reserved.",

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"Cardiovascular manifestations of Takayasu arteritis and their relationship to the disease
activity: Analysis of 204 Korean patients at a single center", "type" : "article-journal", "volume" :
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style-language/schema/raw/master/csl-citation.json" }} Furthermore 18% develop moderate to

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severe aortic regurgitation, providing an additional role for the inclusion of CMR within the WB-MRA protocol in this cohort. The feasibility of WB-MRA in this clinical setting this has been described in a previous study of 8 patients with TA where it was able to locate and quantify the full burden of disease.

{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1", "itemData" : { "DOI" : "10.1007/s00380-006-0918-0", "ISBN" : "8621640384", "ISSN" : "0910-8327", "PMID" : "17143719", "abstract" : "Using a 1.5-T magnetic resonance (MR) imager equipped with 32 receiving channels and integrated parallel acquisition techniques, 37 patients underwent whole-body three-dimensional (3D) contrast-enhanced MR angiography (WB 3D CE MRA). The patients included had clinically documented or suspected peripheral arterial occlusive disease (PAOD, n = 19), Takayasu arteritis (n = 8), polyarteritis nodosa (n = 1), type-B dissection (n = 4), thoracic and/or abdominal aneurysm (n = 5). Sixty-eight surface coils were employed to encompass the whole body. Four 3D CE MRA stations were acquired successively through automatic table moving. The spatial resolution was 1.6 x 1.0 mm and slice thickness was 1.5 mm for all stations. A total scan range of 188 cm was acquired. Overall image quality of each arterial segment and venous overlay were assessed. The depiction of various systemic arterial diseases was evaluated and compared, in 20 patients, with other imaging modalities. This WB 3D CE MRA yielded a detailed display of the arterial system with an average MR room time of 17.4 min. The image quality was considered diagnostic in 99.3% of the arterial segments. In 7 of 19 patients with PAOD, WB MRA showed additional vascular narrowing apart

from peripheral arterial disease. In nine patients with vasculitis, WB MRA depicted luminal irregularity, narrowing or occlusion, aneurysm, and collateral circulation involving multiple vascular segments. WB MRA also clearly revealed the severity and extent of dissection and aortic aneurysm. In 20 cases where additional imaging investigations have been carried out, the vascular pathologies demonstrated by WB MRA agree with these additional imaging investigations.", "author" : [ { "dropping-particle" : "", "family" : "Lin", "given" : "Jiang", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Chen", "given" : "Bin", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Wang", "given" : "Jian-Hua", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Zeng", "given" : "Meng-Su", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" }, { "dropping-particle" : "", "family" : "Wang", "given" : "Yi-Xiang", "non-dropping-particle" : "", "parse-names" : false, "suffix" : "" } ], "container-title" : "Heart and vessels", "id" : "ITEM-1", "issue" : "6", "issued" : { "date-parts" : [ [ "2006", "11" ] ] }, "page" : "395-8", "title" : "Whole-body three-dimensional contrast-enhanced magnetic resonance (MR) angiography with parallel imaging techniques on a multichannel MR system for the detection of various systemic arterial diseases.", "type" : "article-journal", "volume" : "21" }, "uris" : [ "http://www.mendeley.com/documents/?uuid=457c1358-2b09-4466-9ca3-087f9fe44ede" ] } ], "mendeley" : { "formattedCitation" : "<sup><sup>61</sup></sup>",

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"<sup><sup>61</sup></sup>" }, "properties" : { }, "schema" : "https://github.com/citation-

style-language/schema/raw/master/csl-citation.json" }} GCA has a similar prevalence of thoracic,

abdominal and renal involvement to TA, but has a higher prevalence of aneurysmal vascular

involvement with 62% of the vessels involved demonstrating aneurysmal dilation.{ADDIN

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cell arteritis (GCA) and Takayasu arteritis (TAK) have been considered distinct disorders based

on their clinical features, age of onset, and ethnic distribution. However, on closer examination,

these disorders appear more similar than different. The histopathology of arterial lesions in

these diseases may be indistinguishable. Imaging studies have revealed large vessel

inflammation in at least 60% of patients with GCA. We questioned whether the distinctions

between these diseases might in part be an artifact due to bias in gathering historical and

physical data. We postulated that signs and symptoms of GCA and polymyalgia rheumatica

occur in patients with TAK but have been under-reported as a result of this bias.We performed

a retrospective review of 75 patients with TAK and 69 patients with GCA (per American College

of Rheumatology criteria). Signs and symptoms attributable to disease within the year before

and following diagnosis, treatment and interventional outcomes, and mortality were recorded

using a standardized database. All cases were evaluated by a single physician, using identical

history and physical examination forms for patients with both diseases. Patients were predominantly female (TAK 91%, GCA 82%) and white (TAK 88%, GCA 95%). New headache was a presenting symptom in 52% of TAK and in 70% of GCA patients. All TAK patients underwent vascular imaging studies and were demonstrated to have large vessel abnormalities. However, only a subset of patients with GCA (43/69, 62%) was similarly studied. Among this group, 73% of GCA patients had at least 1 arterial lesion identified. In both TAK and GCA, the most common sites of involvement were the aorta (TAK 77%, GCA 65%) and subclavian (TAK 65%, GCA 37%) arteries. Compared to patients with TAK, patients with GCA had a greater prevalence of jaw claudication (GCA 33%, TAK 5%), blurred vision (GCA 29%, TAK 8%), diplopia (GCA 9%, TAK 0%), and blindness (GCA 14%, TAK 0%). Symptoms, signs, and imaging abnormalities that are characteristic of GCA or TAK are often present, albeit in differing frequencies, in both disorders. These findings lend support to the hypothesis that these diseases may not be distinct entities, but represent skewed phenotypes within the spectrum of a single disorder. Differences in frequencies of manifestations may reflect a significant bias in how data are gathered for patients with each disease, as well as the influence of vascular and immunologic senescence.

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style-language/schema/raw/master/csl-citation.json" }} Thus when reviewing this cohort use of the raw data rather than the subtracted data is needed to ensure partially thrombosed aneurysms with a preserved luminal diameter are not missed. Use of the raw data will also allow for assessment of vascular wall thickening.

### Fibromuscular dysplasia

Fibromuscular dysplasia is a non-inflammatory vasculitide which afflicts predominantly young women, causing vascular stenosis, aneurysms and tortuosity.{ADDIN CSL\_CITATION {

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(FMD) is a nonatherosclerotic noninflammatory vascular disease that primarily affects women

from age 20 to 60, but may also occur in infants and children, men, and the elderly. It most commonly affects the renal and carotid arteries but has been observed in almost every artery in the body. FMD has been considered rare and thus is often underdiagnosed and poorly understood by many health care providers. There are, however, data to suggest that FMD is much more common than previously thought, perhaps affecting as many as 4% of adult women. When it affects the renal arteries, the most common presentation is hypertension. When it affects the carotid or vertebral arteries, the patient may present with transient ischemic attack or stroke, or dissection. An increasing number of patients are asymptomatic and are only discovered incidentally when imaging is performed for some other reason or by the detection of an asymptomatic bruit. FMD should be considered in the differential diagnosis of a young person with a cervical bruit; a "swishing" sound in the ear(s); transient ischemic attack, stroke, or dissection of an artery; or in individuals aged >35 years with onset hypertension. Treatment consists of antiplatelet therapy for asymptomatic individuals and percutaneous balloon angioplasty for patients with indications for intervention. Patients with aneurysms should be treated with a covered stent or open surgical repair. Little new information has been published about FMD in the last 40 years. The recently instituted International Registry for Fibromuscular Dysplasia will remedy that situation and provide observational data on a large numbers of patients with FMD. ?? 2011 Society for Vascular Surgery.", "author" : [ { "dropping-particle" : "", "family" : "Olin", "given" : "Jeffrey W.", "non-

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 "<sup><sup>63</sup></sup>", "properties" : { }, "schema" : "https://github.com/citation-  
 style-language/schema/raw/master/csl-citation.json" }} Given the young age that this disease  
 typically affects, MRA is the ideal modality for the assessment of this. The typical presentation  
 is with persistent hypertension in a young woman and an angiographic finding of a string of  
 beads within the renal arteries. However a recently published registry of 921 patients with  
 FMD revealed a high frequency and geographically diverse range of vascular involvement with  
 22% having aneurysms and 26% having dissections.{ADDIN CSL\_CITATION { "citationItems" : [ {  
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 "27386771", "abstract" : "Background Fibromuscular dysplasia (FMD) is a noninflammatory  
 arterial disease that predominantly affects women. The arterial manifestations may include  
 beading, stenosis, aneurysm, dissection, or tortuosity. Objectives This study compared the



frequency, location, and outcomes of FMD patients with aneurysm and/or dissection to those of patients without. Methods The U.S. Registry for FMD involves 12 clinical centers. This analysis included clinical history, diagnostic, and therapeutic procedure results for 921 FMD patients enrolled in the registry as of October 17, 2014. Results Aneurysm occurred in 200 patients (21.7%) and dissection in 237 patients (25.7%); in total, 384 patients (41.7%) had an aneurysm and/or a dissection by the time of FMD diagnosis. The extracranial carotid, renal, and intracranial arteries were the most common sites of aneurysm; dissection most often occurred in the extracranial carotid, vertebral, renal, and coronary arteries. FMD patients with dissection were younger at presentation (48.4 vs. 53.5 years of age, respectively;  $p < 0.0001$ ) and experienced more neurological symptoms and other end-organ ischemic events than those without dissection. One-third of aneurysm patients (63 of 200) underwent therapeutic intervention for aneurysm repair. Conclusions Patients with FMD have a high prevalence of aneurysm and/or dissection prior to or at the time of FMD diagnosis. Patients with dissection were more likely to experience ischemic events, and a significant number of patients with dissection or aneurysm underwent therapeutic procedures for these vascular events. Because of the high prevalence and associated morbidity in patients with FMD who have an aneurysm and/or dissection, it is recommended that every patient with FMD undergo one-time cross-sectional imaging from head to pelvis with computed tomographic angiography or magnetic resonance angiography.", "author" : [ { "dropping-particle" : ""

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The extra-cranial carotid, renal, and intra-cranial arteries were the most common sites of aneurysm, while dissection most often occurred in the extra-cranial carotid, vertebral, renal, and coronary arteries. Iliac and popliteal disease was also found but less common. As a result a recommendation was made for full vascular imaging in all FMD patients. The high rate of intracranial abnormalities would suggest for the augmentation of the standard WB-MRA technique with an intracranial TOF angiogram to yield maximum benefits. Additional coronary specific sequences for coronary dissection could be considered and case reports have shown the ability to detect intramural haematoma in those with spontaneous dissection, however the sensitivity and specificity of this technique has not been established.

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## **Conclusion**

Significant advances in MRI technology has allowed for the extension of traditional single site MRA to include the entire vasculature in a single examination. Vascular disease is frequently a systemic disorder therefore a systematic approach to the detection and quantification of this may better diagnose and stratify these. WB-MRA is a technique that can be incorporated into the routine clinical workflow, provides a systematic approach to the assessment of vascular disease in a single examination, and yields a high degree of clinically occult but significant vascular disease. Future work is required to determine how best to utilize the information provided to optimise management of vascular disease.

**References**

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**Table 1:** Injection protocols available in the literature for the dual bolus injection technique.

\*all protocols use a 10-30ml saline bolus to immediately follow each contrast injection

	First injection*	Second injection*
0.5M Gadolinium based contrast agent		
1.5T	20ml at 1ml/s	20ml at 1ml/s
3T standardised	10ml at 1ml/s	15ml at 1.5ml/s
3T weight adjusted (0.3mmol/kg)	40% total volume at 1ml/s	60% total volume at 1ml/s

1.0M Gadolinium based contrast agent		
1.5T  (0.2 mmol/kg diluted to 60ml)	Biphasic injection protocol: 1.3  ml/s and 0.7 ml/s	



**Table 2:** Image acquisition parameters at 3T for a combined whole body angiography and cardiac MRI protocol. Amended from Gandy et al.

**AIM** To evaluate a combined protocol for simultaneous cardiac MRI (CMR) and contrast-enhanced (CE) whole-body MR angiography (WB-MRA) techniques within a single examination.

**MATERIALS AND METHODS** Asymptomatic volunteers (n = 48) with low-moderate risk of cardiovascular disease (CVD) were recruited. The protocol was divided into four sections: (1) CMR of left ventricle (LV) structure and function; (2) CE-MRA of the head, neck, and thorax followed by the distal lower limbs; (3) CMR LV  $\text{w}^{\text{late}}$  gadolinium enhancement  $\text{w}^{\text{late}}$  assessment; and (4) CE-MRA of the abdomen and pelvis followed by the proximal lower limbs. Multiple observers undertook the image analysis.

**RESULTS** For CMR, the mean ejection fraction (EF) was  $67.3 \pm 4.8\%$  and mean left ventricular mass (LVM) was  $100.3 \pm 22.8$  g. The intra-observer repeatability for EF ranged from 2.1-4.7% and from 9-12 g for LVM. Interobserver repeatability was 8.1% for EF and 19.1 g for LVM. No LV delayed myocardial enhancement was observed. For WB-MRA, some degree of luminal narrowing or stenosis was seen at 3.6% of the vessel segments (involving n = 29 of 48 volunteers) and interobserver radiological opinion was consistent in 96.7% of 1488 vessel segments assessed.

**CONCLUSION** Combined assessment of WB-MRA and CMR can be undertaken within a single examination on a clinical MRI system. The associated analysis techniques are repeatable and

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Description	WB-MRA	WB-MRA	CARDIA C	CARDIA C	CARDIA C	WB-MRA	WB-MRA
Location	Station 1	Station 4	Heart	Heart LV	Heart LV	Station 2	Station 3
Sequence	3D TurboFLAS H	3D TurboFLAS H	2D bSSFP	2D bSSFP	2D PSIR	3D TurboFLAS H	3D TurboFLAS H
Cardiac Phases	-	-	25	25	-	-	-
ECG Gating	-	-	Retro	Retro	Pro	-	-
Lines/segment	-	-	14	26	25	-	-
Orientation	Coronal	Coronal	4ch, 3ch & 2ch	SA	SA	Coronal	Coronal
TR/TE (ms)	2.68/1.00	2.61/0.96	3.37/1.48	3.40/1.50	5.21/1.99	2.60/0.96	3.47/1.21
FA (°)	19	22	>50	>50	20	16	37
FOV (mm)	360x500	360x500	>360	>360	>360	344x500	344x500
Phase FOV (%)	71.9	68.8	84.4	84.4	75.0	68.8	71.9
Slice (mm)	1.1	1.0	6.0	6.0	6.0	1.3	1.4
Number Slices	96	80	1	2	2	96	96
Matrix (pix)	313x512	277x448	216x256	173x256	144x256	264x512	242x448
Voxel Size (mm)	1.0x0.8x1.1	1.1x1.1x1.4	Variable	Variable	Variable	1.1x0.9x1.0	1.0x0.9x1.3
Parallel	x3	x3	x2	x2	x2	x3	x3

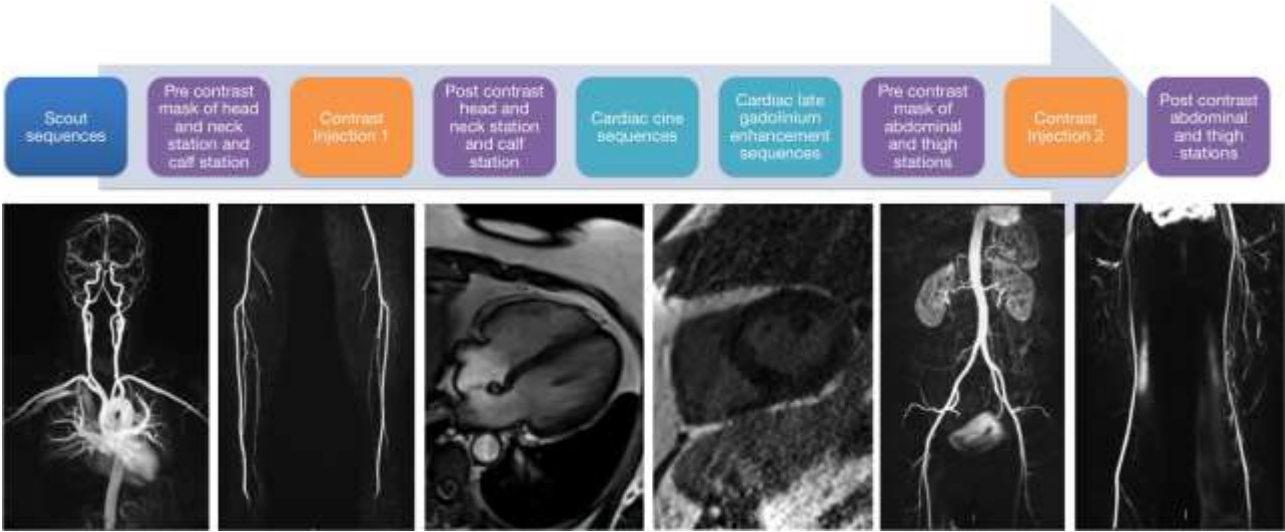
Imaging							
K-space	Linear	3D centric	Linear	Linear	Linear	3D centric	3D centric
BW (Hz/pix)	700	700	930	930	287	700	740
Scan Time (Sec)	18	14	<20	<20	<20	14	16

Abbreviations used are as follows: bSSFP = balanced steady state recovery; BW = Bandwidth; FA = Flip Angle; FOV = Field of View; i-PAT = integrated Parallel Acquisition Technique; LV = left ventricle; Pro = Prospective; Pix = Pixels; PSIR = Phase Sensitive Inversion Recovery; Retro = Retrospective; SA = Short Axis; Slice = Slice Thickness; TE = Echo Time; TR = Repetition Time; 2ch = Two Chamber; 3ch = Three chamber; 4ch = Four Chamber.

**Figure 1:** Body coil set-up for performing a whole body magnetic resonance angiogram.



**Figure 2:** Schematic of the order of sequence acquisition for integrated whole body magnetic resonance angiogram and cardiac MRI.



**Figure 3:** Selection of incidental findings on WB-MRA including a cerebral arteriovenous malformation (arrow), inflammatory arthritis (arrow head) and lung malignancy (\*).



**Figure 4:** Example of a whole body atheroma scoring system. The Whole Body MRA is

separated into 31 vessels (described on the right) with each scored according to their degree of stenosis. This score is then summated, normalized to the number of assessable segments and then divided by four and expressed as a percentage of the maximum possible score.

Adapted from Duce et al.{ADDIN CSL\_CITATION { "citationItems" : [ { "id" : "ITEM-1",

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disease without diabetes [10.1 (0-39.5)], followed by those with T2DM and CVD [4 (0-41.1)], then those with T2DM only [3.23 (0-19.4)] with healthy controls having the lowest atheroma score [2.4 (0-19.4)]. Both groups with a prior history of CVD had a higher SAS and left ventricular mass than those without ( $p < 0.001$  for both). However after accounting for known cardiovascular risk factors, only the SAS in the group with CVD without T2DM remained significantly elevated. 6 % of the T2DM group had evidence of silent myocardial infarct, with this subcohort having a higher SAS than the remainder of the T2DM group [7.7 (4-19) vs. 2.8 (0-17),  $p = 0.024$ ].

**CONCLUSIONS** Global atheroma burden was significantly higher in those with known cardiovascular disease and without diabetes but not in those with diabetes and cardiovascular disease suggesting that cardiovascular events may occur at a lower atheroma burden in diabetes.

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### Head and neck

Left and right internal carotid; Left and right vertebral; Innominate; Left and right common carotid; Left and right subclavian

### Aorta

Aortic arch; Thoracic aorta; Abdominal aorta

### Abdominal

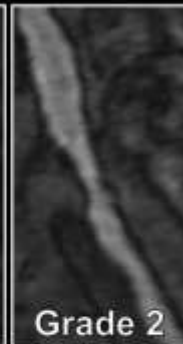
Coeliac trunk; Superior mesenteric; Inferior mesenteric; Left and right renal

### Iliofemoral

Left and right common, external and internal iliac; Left and right superficial and common femoral; Left and right profunda femoris

### Popliteal and infrageniculate

Left and right popliteal; Left and right anterior tibial; Left and right peroneal; Left and right posterior tibial



$$\text{Atheroma Score} = [ (\sum \text{MRA score} / n) \div 4 ] \times 100$$

**Figure 5:** Peripheral arterial disease patient with multisite disease revealed by WB-MRA. A- Whole body angiogram. B - Sagittal MIP showing >50% stenosis of the internal carotid artery (arrow head). C - Coronal MIP of the renal arteries showing a normal right renal artery but a >70% stenosis of the left renal artery (arrow head). D - Coronal MIP showing a long segment occlusion of the left superficial femoral artery (arrow) with extensive collateral formation (arrow heads). E- Short axis late gadolinium enhancement showing a large unrecognised myocardial infarct (arrow head). F – 4 chamber view of the heart showing normal dimensions of the ventricles. Reproduced from Weir-McCall et al.

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